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ON THE DECOMPOSITION OF THE LEUCOSULPHONIC ACIDS OF ROSANILINE HYDROCHLORIDE AND CRYSTAL-VIOLET IN AQUEOUS SOLUTION.

BY J. H. KASTLE.

The fact that the coloring matters of certain flowers can be bleached by sulphur dioxide has been known for a long time. Through the researches of Schoenbein¹ on this subject it was established that the color of indigo and the coloring matter of certain flowers, such as that of the purple dahlia, which had been bleached by means of sulphur dioxide can be restored by means of acids and alkalies, by methyl and ethyl alcohols, and by oil of bitter almonds; by oxidizing agents such as ozone, ozonized turpentine, chlorine, bromine, iodine, and hypochlorites; by hydrogen sulphide; and, most remarkable of all, by heating to 100° C., and even by cooling to low temperatures by freezing mixtures. Thus he was able to alternately color and bleach a rose, which had been bleached in sulphur dioxide, no less than thirty times in one minute by

¹ Schoenbein: *Verh. Naturf. Ges., Basel*, **1**, 5-8 11-13, 13-16 (1854-1857); **2**, 15-20 (1858-1860).

alternately heating and cooling it in an atmosphere of hydrogen.

In 1905 Kastle¹ confirmed a number of these earlier observations, and pointed out that the affinities of acids can be determined colorimetrically by means of certain vegetable coloring matters which had been bleached by means of sulphur dioxide. Later Kastle and Amoss² employed a solution of the coloring matter of the red cabbage (*Brassica oleracea*) which had been bleached by means of sulphur dioxide as a reagent for the detection of free hydrochloric acid in gastric contents and its estimation colorimetrically.

The principal difficulty which has been encountered in the use of such reagents is that they are unstable and hence have to be prepared fresh from time to time, and the materials employed can be obtained only at certain seasons of the year. Attempts have therefore been made by the writer from time to time during the past two or three years, though without success, to find an artificial coloring matter, the sulphurous acid leuco-compound of which would conduct itself towards acids as do the corresponding leuco-compounds of certain of the vegetable coloring matters. Such being the case I have recently had one of the assistants in the Hygienic Laboratory, Mr. F. A. McDermott, try the action of sulphurous acid on a large number of artificial dyes. A few of the dyes thus far tested have been found to be bleached by sulphur dioxide. Thus far, however, we have failed to find an artificial dye whose sulphurous acid leuco-derivative is decomposed by acids with the regeneration of the original color.

It has been found, however, that certain dyes of the pararosaniline hydrochloride type yield colorless aqueous solutions when treated with sulphur dioxide, and that the color of such solutions is restored by boiling off the sulphur dioxide. Similar results were obtained by Schoenbein³ in his work on the action of sulphur dioxide on cyanine (quinoline-blue). He showed that moist cyanine paper is rapidly bleached by sulphur dioxide, and that on exposure to the air such bleached cyanine

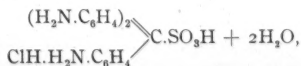
¹ THIS JOURNAL, **33**, 46-59 (1905).

² P. Am. Soc. Biol. Chem., **1**, 20-21 (1907).

³ Verh. Naturf. Ges., Basel, **4**, 215-218 (1864-1867).

paper rapidly turns blue, and that on the same strip of paper this alternate bleaching and bluing may be observed in rapid succession by exposing the paper first to sulphur dioxide and then to air. According to this author the cause of the bluing of the bleached cyanine paper lies in the instability of the colorless compound, which is so great that sulphur dioxide is given off from it even at ordinary temperatures, in much the same way that ammonia and carbon dioxide are given off from ammonium carbonate.

It therefore occurred to me that aqueous solutions of such leuco-compounds would, in all probability, exhibit the phenomenon of dissociation by heat. As a matter of fact my experiments with the leucosulphonic acids of rosaniline hydrochloride and crystal-violet indicate that such is really the case. Our knowledge of these compounds dates from 1867, when Schiff¹ prepared the so-called fuchsine-sulphurous acid and recommended its use as a reagent for aldehydes. The leuco-compound resulting from the action of sulphur dioxide on fuchsine (pararosaniline hydrochloride) was first isolated in pure condition by Hantzsch and Osswald.² According to these authors this compound, to which they have given the name "Pararosaniline-hydrochloride-leucosulphonic acid," has the constitution



and when first prepared is colorless and crystalline, but on drying it becomes faintly red. They called attention to its instability and to the ease with which it is resolved into its components; thus they observed that sulphur dioxide is partially expelled from the compound by a current of carbon dioxide even in the cold, whereby the coloring matter (pararosaniline hydrochloride) is regenerated. They also accounted for the difficulty and failure on the part of other chemists to obtain the acid as due partly to the instability of the compound and partly to the sparing solubility of fuchsine in water.

¹ Bull. Soc. Chim., [1] 7, 518 (1867); Compt. Rend., 64, 182 (1867).

² Ber. d. chem. Ges., 33, 310-311 (1900).

A few years later, Dürschnabel and Weil¹ also investigated the action of sulphurous acid on certain triphenylmethane coloring matters. In their work, however, they employed the free bases of these dyes, not the salts, and while the derivatives they obtained are of great interest, they differ essentially in composition, constitution and properties from the sulphurous acid derivatives of the salts of the dyes of the pararosaniline type described by Hantzsch and Osswald,² and hence warrant no further consideration in this connection.

So far as I have been able to discover, no observations have been recorded by the above-named chemists or by others on the decomposition of the leucosulphonic acids of the dyes of the pararosaniline hydrochloride type in aqueous solution. That aqueous solutions of such compounds are readily decomposed by heat is indicated by the following observations:

Dilute solutions of rosaniline hydrochloride and crystal-violet, containing about 0.05 gram of the dye in 50 cc. of water, were decolorized by means of sulphur dioxide. Such solutions may be preserved unchanged in glass-stoppered bottles, under ordinary conditions prevailing in the laboratory, for several days, and possibly for longer intervals. The mouths and necks of the bottles, however, gradually show the colors of the dyes in their original tints, *viz.*, red and violet. Similarly if a drop of these colorless solutions be placed upon filter paper, a red or blue ring gradually appears as the solutions evaporates, and pieces of linen or cotton cloth may be dyed red or blue by immersion in these solutions and drying in the air. So, also, if these colorless solutions are boiled for a long time so as to remove the sulphur dioxide, deep bluish-violet and red solutions are obtained whose colors are permanent. Obviously these changes of color result from the decomposition of the unstable leucosulphonic acids, either spontaneously as the result of the action of heat, or through the action of the oxygen or carbon dioxide of the air, or as the result of the combined action of heat and water. On the other hand, if the colorless solutions of the leucosulphonic acids of these dyes be boiled

¹ Ber. d. chem. Ges., **38**, 3492-3496 (1905).

² *Loc. cit.*

for only a short time, in order not to remove all of the sulphur dioxide, the solutions become colored red and blue, respectively, and these colors persist as long as the solutions remain hot. If now they be cooled by plunging the tubes into cold water, the colors fade rapidly and the solutions again become colorless. These changes, as brought about by the alternate heating and cooling, have been repeated several times on the same solution. In such cases, therefore, it would seem either that the oxygen or carbon dioxide of the air did not act through a sufficiently long interval to completely decompose these leucocompounds, or that these color changes were the result of the dissociation of the leucosulphonic acids by heat, or of their hydrolytic dissociation.

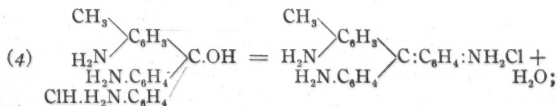
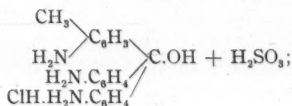
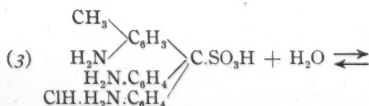
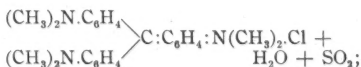
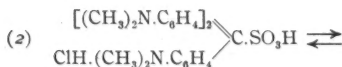
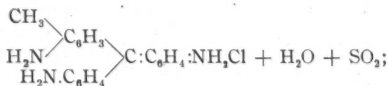
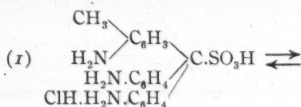
In order to throw further light on these phenomena, a number of sealed tubes were prepared containing about three cubic centimeters of the colorless solutions of these leucocompounds, the space above the liquid in the tube, about 6 cc., being filled with air. These tubes were then placed in boiling water. In from one to two minutes, the solutions had become red and bluish-violet, respectively. When the hot tubes were immersed in cold water, the colored solutions bleached rapidly, 30 seconds to one minute being required for complete decolorization. With the tubes first prepared for this purpose, these phenomena, *viz.*, coloration by heating to $100^{\circ}\text{C}.$, and decolorization by cooling to ordinary temperatures, have been repeated fifteen times, and after standing under ordinary laboratory conditions for two days, the tubes were found to be as sensitive to the effect of heat and cold as they were when first prepared.

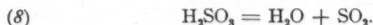
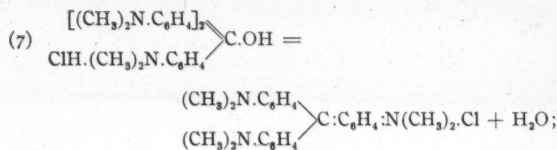
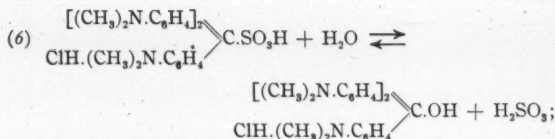
In order to exclude the effect of carbon dioxide or oxygen of the air on the changes under consideration, three tubes or glass bulbs were prepared, containing small amounts of the leucosulphonic acid of crystal-violet, and labeled No. 1, No. 2, and No. 3. Tube No. 1 was then connected with the vacuum pump for fifteen minutes; under the influence of the vacuum, considerable amounts of sulphur dioxide boiled off, the effect of which, together with that of the vacuum, was certainly to remove all except the merest traces of oxygen

and carbon dioxide. The tube, while still connected with the pump, was sealed in the flame of the blowpipe. Through Tube No. 2, a current of hydrogen was passed in order to drive out all of the air, and the tube sealed in the flame while the current of hydrogen was still passing through it. Tube No. 3, which was in the form of a bulb with a long narrow neck, 1 to 2 mm. in diameter, was filled with the solution of the leucosulphonic acid of crystal-violet to a point very near the orifice, and heated in a bath of boiling water for five minutes. Under these conditions, the sulphur dioxide and the overflow from the liquid, due to expansion by heat, displaced the air. The tube was then sealed in the flame while still in the bath of boiling water. On heating in a bath of boiling water, the solutions contained in these three tubes became deep bluish-violet in color in from 30 seconds to one minute, this change from colorless to bluish-violet occurring first on the upper surface and in the upper layers of the liquid. On immersion in cold water, Tube No. 3 became colorless in from 30 seconds to one minute; Tubes Nos. 1 and 2 required a longer time to decolorize completely, usually 20 to 30 minutes, but at the end of this time, neither showed the slightest trace of color. On the day on which these tubes were prepared, these phenomena were repeated a number of times, and on the following day they were repeated again. Three days later these tubes showed precisely the same changes of color on heating and cooling that they showed on the day on which they were prepared, and after an interval of forty days they still showed the same changes of color on heating and cooling.

It is evident, therefore, that the decomposition of the leucosulphonic acids of the dyes of the pararosaniline type, in aqueous solution, is a reversible process and that atmospheric air is not responsible for the changes of color observed when such solutions are heated and cooled. Whether the change in question is one of simple dissociation by heat, as indicated in equations (1) and (2), or whether it is a hydrolytic dissociation, as indicated by equations (3), (4), (5), (6), (7) and (8), can only be determined by quantitative

measurements, which will require more time than I can devote to the subject at present. My own opinion is that the latter view is more probable and that the change in question is one of hydrolytic dissociation. This I hope to demonstrate by quantitative measurements at the first opportunity.





In support of the view that the changes observed on heating aqueous solutions of these leucosulphonic acids are due to dissociation, simple or hydrolytic, may be mentioned the fact that the production of the dye by the action of heat takes place first on the upper surface and in the upper layers of the liquid, and that the larger the amount of sulphur dioxide present in the solution of the leucosulphonic acid of the dye, the smaller the quantity of coloring matter produced on heating the solution and the more rapid the bleaching of the colored liquid on cooling, indicating, as might be expected if these changes are due simply to dissociation, that an excess of one of the products of the dissociation depresses the decomposition to a certain extent, and correspondingly hastens the formation of the leucosulphonic acid from the products of the decomposition.

The strikingly beautiful character of these color changes and the ease with which aqueous solutions of the leucosulphonic acids of these dyes can be prepared and handled are such as to render these compounds especially useful on the lecture table for the illustration of reversible phenomena.

[Contribution from Kent Chemical Laboratory of the University of Chicago.]

ON THE ACTION OF FEHLING'S SOLUTION ON MALT SUGAR.

By W. LEE LEWIS.

The following pages contain a report of a preliminary and incomplete investigation carried out by myself, at the suggestion and under the direction of Dr. Nef, of the products formed in the oxidation of malt sugar by alkaline solutions containing cupric hydroxide (Fehling's solution). The work shows that the ratio of the various acids—carbonic, formic, glycollic, hexonic, and probably glycerinic and trioxybutyric—formed in this oxidation differs very decidedly from that observed by Nef¹ in the case of dextrose, laevulose, and mannose, respectively. Furthermore, a new hexonic acid, probably α -oxymethyl-*d*-ribonic, is formed in the case of maltose in place of α -oxymethyl-*d*-arabonic acid.² Whereas the simple hexoses named give *d*-gluconic and small amounts of *d*-mannonic acid, malt sugar gives large quantities of glucosido-*d*-mannonic acid only, for reasons already emphasized by Nef.³ It is certain also that oxidation of maltose by Fehling's solution is not accompanied by any very appreciable hydrolysis into two molecules of *d*-glucose, the main oxidation products formed in this case being glucosido monobasic acids whose separation as such cannot as yet be accomplished. A slight splitting of maltose into two molecules of dextrose before oxidation may possibly occur, since the subsequent hydrolysis of the glucosido acids formed always gave less dextrose than would result if only one-half of the malt sugar molecule, *i. e.*, the aldehyde portion, $C_6H_{12}O_6$, $CH_2OH-CHOH-CHOH-CHOH-CHOH-CHO$, had been oxidized. Thus the hydrolysis of the glucosido acids obtained from 24 grams of maltose which are not affected by boiling Fehling's solution gave in four independent experiments, on heating for 10 hours at 100° with five per cent. sulphuric

¹ Nef: Ann. Chem. (Liebig), **357**, 259.

² Nef: Ann. Chem. (Liebig), **357**, 298; Thesis of H. A. Spoehr soon to be published in THIS JOURNAL.

³ Nef: Ann. Chem. (Liebig), **357**, 232.

acid, a mean of 10.145 grams of *d*-glucose, and three similar experiments with 144 grams of maltose gave 47.67 grams, 55.04 grams, and 48.40 grams dextrose, respectively. Assuming that the malt sugar used contained the usual quantity, one molecule, of crystal water, the amount of *d*-glucose theoretically possible on subsequent hydrolysis of the glucosido acids would be exactly one-half of the sugar originally used. When we bear in mind, however, that *d*-glucose itself is not entirely unchanged on heating with 5 per cent. sulphuric acid at 100°, it is clear from the above statement of facts that the malt sugar molecule oxidizes mainly as such with Fehling's solution, giving glucosido acids. These latter are of especial interest because of their possible bearing on the constitution of malt sugar itself. Furthermore, the well-known fact that one molecule of dextrose, $C_6H_{12}O_6$, takes up 2.48 atoms of oxygen, whereas one molecule of maltose, $C_{12}H_{22}O_{11}$, requires only 2.86 atoms when treated with Fehling's solution, now demands no further explanation.

Perhaps the most striking contrast to be noticed between malt sugar, on the one hand, and the simple hexoses—dextrose, laevulose, and mannose—on the other, is the marked difference in the relative amounts of formic and carbonic acids formed in the treatment with the reagent named. One hundred grams of malt sugar gave 3.60 grams of formic acid and 7.37 grams of carbon dioxide, whereas 100 grams of a simple hexose gave from 2.0 to 4.0 grams of carbon dioxide and from 12.0 to 14.0 grams of formic acid.¹

The following further difference is also noteworthy: Mannose, dextrose and laevulose gave, besides glycollic and hexonic acids, large amounts of glycerinic and trioxybutyric acids. In the case of maltose, I was unable to establish (by hydrolysis) with certainty the presence of any monobasic acids containing three or four carbon atoms.

It is therefore already certain that the aldehyde portion of the maltose molecule must be oxidized, under the conditions named, in a manner considerably different from that of the oxidation of simple aldohexoses. It would, however,

¹ Nef: Ann. Chem. (Liebig), **357**, 259.

be premature to develop any theory on this point until certainty has been gained as to the complete nature and relative amounts of the various oxidation products formed from malt sugar.¹

EXPERIMENTAL PART.

Six 24-gram lots of Kahlbaum's maltose, melting at 106°-112°, were worked up in the following manner: Twenty-four grams of maltose were dissolved in 70 cc. of water, and solutions containing 95.6 (2.86 mols. O) grams of hydrated copper sulphate in 300 cc. and 181.0 grams of crystallized barium hydroxide in 750 cc. of water were also prepared. The quantity of copper sulphate used was that just reduced by the 24 grams of maltose under the conditions, and is practically identical with the ratio in use in titrating maltose with Fehling's solution in the usual manner. The barium hydroxide taken was one and a half molecules, calculated against the copper sulphate. Preliminary attempts with three molecules of sodium hydroxide in place of the barium hydroxide failed because of the difficulty of recovering the acids quantitatively from the resulting salt mixture.

All three solutions were heated to boiling and the unfiltered barium hydroxide solution was added slowly with active shaking to the solution of copper sulphate. The hot solution of sugar was similarly added to the mixture and the whole heated in a boiling water bath for one hour with occasional shaking. Reduction, which always started immediately and proceeded rapidly, was complete in this time, as evidenced in the almost entire disappearance of the copper-blue color from the solution. The calculated amount of sulphuric acid was now added, the mixture filtered, and the well-washed, bulky precipitate twice taken up and boiled in 500 cc. of water containing two grams of sulphuric acid. The collected filtrates, which showed no reduction of Fehling's solution, were freed from copper by saturation with hydrogen sulphide, then a very slight excess of barium added, and the water

¹ Work on the further determination of the nature of the products formed from maltose by Fehling's solution, as well as by the oxidation of alkaline solutions of malt and milk sugar by air and by hydrogen peroxide, is at present being continued by Dr. Nef and his students in this laboratory.

and volatile formic acid distilled off at 12 to 25 mm. pressure, the solution being finally heated for one-half hour on the boiling water bath. The residue of acids appeared as a golden brown, slightly mobile syrup. Six such operations with a total of 144 grams of maltose, corresponding to 136.8 grams of the anhydrous sugar, gave 132.8 grams of nonvolatile acids.

Determination of Carbon Dioxide.—Carbon dioxide was determined in independent experiments as follows: Solutions of maltose and copper sulphate were prepared as at first and also a solution of sodium hydroxide containing 46.1 grams (three molecules) in 400 cc. of water. The solutions were well mixed cold—the alkali with the copper sulphate and the sugar with this mixture—and finally boiled in a water bath for one and one-half hours. After filtering off the cuprous oxide the carbon dioxide was set free with hydrochloric acid, calculated for one-third of the alkali used, and driven out of the solution by heating in a flask connected successively with a reversed condenser and with three tall cylinders filled with a saturated aqueous solution of barium hydroxide. The acid was added slowly by means of a separatory funnel, and to insure complete expulsion of the soluble gases, the liquid was finally heated in a bath at 110°–120° for two hours. During the experiment, air freed from carbon dioxide was drawn slowly through the solution. The precipitated barium carbonate was then filtered off, well washed, and dried at 100°. Control experiments were run for the amount of carbon dioxide in the reagents used, and proper deductions made. Twenty-four grams of sugar gave 7.93 grams of barium carbonate, corresponding to 1.77 grams of carbon dioxide.

Determination of Volatile Acids.—The distillates from each 24-gram lot of maltose, amounting to 3.5–4 liters, were separately made up to definite volume and an aliquot portion titrated with N/10 sodium hydroxide and phenolphthalein as an indicator. These results were checked by the method of H. C. Jones¹ for determining formic acid quantitatively which depends upon its conversion in alkaline solution into

¹ THIS JOURNAL, 17, 537. Cf. Lieben: Monats. Chem., 14, 146; and Péan de St. Gilles: Ann. Chim. Phys., [3] 85, 388.

carbonate with N/10 potassium permanganate. The six distillates averaged 0.790 gram of formic acid with N/10 alkali, and 0.877 gram by Jones's method. These results establish that formic acid is the only volatile acid formed in the experiment, the higher value with permanganate resulting from traces of hydrogen sulphide or other reducing matter carried over in the distillation. Taking the first figures, 144 (138.8 grams of anhydrous sugar) grams of maltose gave 4.740 grams of formic acid.

Determination of Nonvolatile Acids, including Sugar, after Hydrolysis.—The above named residue of nonvolatile syrupy glucosido acids, weighing 132.8 grams, was hydrolyzed by heating under a reflux condenser on the boiling water bath for ten hours with 5 parts of 5 per cent. sulphuric acid. The theoretical amount of barium hydroxide for the removal of the acid was now added, the solution further boiled a half hour, and filtered. After preliminary titrations with Fehling's solution the filtrate was made up to definite volume of approximately one per cent. dextrose content, and accurately titrated for the sugar split off; 50 cc. of Fehling's solution required 24.75 cc. of the 5 liters of filtrate, corresponding to 0.2356 gram of dextrose, or a total of 48.40 grams for the original 132.8 grams of acids.

For the removal of the dextrose the solution was concentrated to 1 liter and boiled in a water bath for 10 hours with 50 grams of powdered calcium carbonate. Twenty-seven grams of undissolved carbonate of lime were filtered off; digestion of this with 5 per cent. acetic acid until there was no further action left an insoluble residue which was dissolved in hydrochloric acid and reprecipitated with ammonia. This gave 0.50 gram of white calcium oxalate; a previous experiment with the same quantities gave 0.9 gram.

Analysis of the salt, dried to constant weight at 100°, gave the following result: 0.4995 gram gave, on ignition, 0.1915 gram CaO.

	Calculated for $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$.	Found.
CaO	38.39	38.35

The aqueous solution of calcium salts and dextrose was concentrated in half-liter hemispherical evaporating dishes and alcohol was added slowly, with thorough stirring. The alcohol was decanted and the process repeated, the black, tarry lime salts being occasionally taken up in water and decolorized with animal charcoal, etc., until finally by precipitation and continued rubbing the salts became granular.¹ After drying they were repeatedly extracted with absolute alcohol until 0.5 gram showed no reduction on boiling with 10 cc. of Fehling's solution. The plate-dried lime salts weighed 107.75 grams and on analysis, by ignition, showed 15.21 per cent. of calcium oxide. The calcium was removed in the usual manner by treating the salts in a hot, dilute solution with a faint excess of oxalic acid. On distilling off the water from the filtrate under reduced pressure, finally heating for one-half hour on the boiling bath, a residue of 82.0 grams of syrupy, slightly mobile acids was obtained, which dissolved entirely in 1 liter of hot, absolute alcohol on long digestion. On concentrating this solution to about 500 cc. there were deposited in 24 hours 12.5 grams of mannonic lactone, melting at 148°-149°. By concentrating the mother liquor, etc., two further crops were obtained, so that finally a total of 22.2 grams of *d*-mannonic lactone were obtained, leaving a residue of 59.8 grams of nonvolatile gummy acids.

A portion of the mannonic lactone dissolved on digestion in 20 parts of absolute alcohol, and on cooling 80 per cent. of the material separated out in the form of light, flaky, snow-white needles. After four crystallizations from absolute alcohol the substance melted at 149°-152° and gave $[\alpha]_{20}^D = +51.5$.² $d = 1.034$; $p = 10.000$, *i. e.*, 1.7186 grams lactone and 15.4674 grams water. $(\alpha) = +5^\circ.34$ in a 1 dem. tube.

The substance gave no change of rotation on standing in water solution 24 hours, and all attempts to raise the specific rotation to that given by Fischer, $+54^\circ.8$, failed.³

Mannonic lactone dissolved in twice its weight of 50 per cent.

¹ E. Fischer: Ber. d. chem. Ges., **22**, 363.

² Fischer: Ber. d. chem. Ges., **22**, 3222. Nef: Ann. Chem. (Liebig), **357**, 270.

³ Cf. Nef: Ann. Chem. (Liebig), **357**, 271.

alcohol yields with an equal amount of phenylhydrazine, on standing 24 hours at room temperature, leafy crystals of the acid hydrazide, melting at 216° . It was also further identified by its conversion into the characteristic brucine salt which separates out from concentrated water solution on addition of alcohol in bulky, silky needles melting at 210° – 212° . The remaining 59.8 grams of nonvolatile, gummy acids were now resolved into three fractions, A, B and C, as follows: They were first dissolved in an equal weight of absolute alcohol, and twice the volume of ether was thereupon slowly added with much shaking. On standing overnight, decanting, and washing the residue with alcohol-ether (1 to 2 by volume) 26.1 grams of thick gum remained undissolved. The soluble portion, 33.8 grams, as well as the insoluble portion, gave on prolonged digestion with acetic ether a total of 25.8 grams of insoluble gum (C). The gums which dissolved in acetic ether were further resolved (after removing the solvent, etc.), by digestion, into an ether-soluble fraction, A, 11.1 grams, and a portion, B, 25.0 grams.

Fraction C (least soluble gums).—This fraction was titrated by the following method, which was uniformly used throughout the work where acids forming lactones were believed to be present. The material was dissolved in water and made up to a convenient volume and an aliquot portion containing about 0.5 gram gum was then taken for titration. This was considerably diluted with water and treated with an excess of N/10 sodium hydroxide for ten minutes on a boiling water bath. The end point was then determined by titrating back with N/10 hydrochloric acid and phenolphthalein as an indicator in all cases. Five-tenths gram of Fraction C required 20 cc. of N/10 alkali. Since half a gram of a hexonic acid lactone requires theoretically 28.07 cc. of N/10 alkali, some neutral material was present, as was shown by subsequent acylation of the fraction. On the basis of this titration the remaining aqueous solution of Fraction C was, however, first digested with the calculated amount, 40.7 grams, of brucine, a small amount of alcohol being added and the mixture boiled for 1 hour on a water bath after the alkaloid had

dissolved. Removal of the water under 20–30 mm. pressure, and finally heating to 80° gave a residue of gummy brucine salts weighing 67.3 grams. After dissolving this in half its weight of water, the subsequent addition of 5 parts of alcohol gave a rapid deposition of crystal needles of *d*-mannonic brucine, 15 grams, melting from 205° to 212°. These, on recrystallization, melted at 210°–212°. Since all attempts to obtain other crystalline brucine salts from the alcoholic filtrate still containing about 50 grams of salts failed, the mixture was converted back into free brucine and acids as follows: A dilute aqueous solution of the salts was treated with an excess, about 1.5 times the calculated amount, of aqueous sodium hydroxide. The precipitated brucine was filtered off and well washed and the remainder was removed from the aqueous filtrate by threefold extraction with chloroform. The filtered alkaline solution was then treated with slightly more than the theoretical amount of aqueous hydrochloric acid and the water removed at 20–30 mm., the solution being finally heated on a boiling water bath. The organic acids were then separated from the salt by thorough extraction with absolute alcohol. In this manner 16.5 grams of acid were finally recovered.

Fraction B.—Five-tenths of a gram of Fraction B, 25 grams, required on titration a total of 37.9 cc. of N/10 alkali; the calculated amount for 0.5 gram 1,2-dioxybutyrolactone is 42.37 cc. The remainder of the aqueous solution of Fraction B was consequently converted into salts by boiling with 76 grams of brucine. Fractional crystallization of the crude salts from small amounts of water and alcohol gave first 11.7 grams of *d*-mannonic brucine melting, after recrystallization, at 210°–212°. This salt can readily be separated from the other high-melting brucine salts of *d,l*-glycerinic, erythronic and threonic acids which may also possibly be present, especially in Fractions A and B, since it comes out very rapidly from hot concentrated aqueous solutions on addition of 4 to 5 volumes of hot alcohol. The 11.7 grams salt mentioned above, as well as the 15 grams of a corresponding salt referred to under Fraction C, were now proved to consist entirely of

d-mannonic lactone as follows: Twenty-four grams of the combined salts gave with sodium hydroxide, etc., 8 grams of crude acid gum (alcohol extract) from which, on crystallization from acetic ether, a total of 5 grams of the lactone melting from 145°–148° was obtained. A portion of this, on further purification, gave crystals melting from 148°–150° and showing a specific rotation of +51.°1; *i. e.*, 2.0012 grams of substance and 18.0087 grams of water, $p = 10.001$; $d = 1.037$, found (α) in 1 dcm. tube, +5.°30.

The portion of the 8 grams of crude lactone which still remained gummy, *i. e.*, about 3.0 grams, gave on treatment with 6 cc. of 50 per cent. alcohol and 3 cc. phenylhydrazine, after 24 hours at ordinary temperatures, 3.7 grams of practically pure *d*-mannonic phenylhydrazide melting from 210° to 216°.

The mother liquors from the above mentioned *d*-mannonic brucine gave, on long standing, a total of 51 grams of crystalline salts, in three crops, which melted from 170° to 205°; and finally the 24.2 grams of gummy noncrystallizable salts left in the mother liquor gave with sodium hydroxide, etc., a total of 9.3 grams acid gum soluble in ethyl acetate. This was united with the corresponding lot, 16.5 grams, of acid gum recovered from Fraction C (see above), and the mixture then further resolved as in the first instance, by fractional precipitation with alcohol and ether, etc., into three fractions, C', 7.1 grams of alcohol extract, least soluble acid gum; B', 10.8 grams gum soluble in acetic ether; and A', 5.0 grams of ether-soluble gum.

Fraction C'.—This portion, 7.1 grams, contained some tar which was removed by acylation as follows: The gum was heated for nine hours at 95°–100° with three parts of acetic anhydride; acetic acid and the excess of acetic anhydride were then removed by distillation at 20 mm. pressure, the flask was finally heated to 100°, and the residue of acylated gums taken up in hot ether, which left some insoluble tar. The acylated gums which had dissolved in the ether were then converted back into the unchanged free acids by threefold hydrolysis with three parts of water, heating for 9 hours at

100° and taking care to remove water and acetic acid after each operation by distilling at 20 mm. pressure and 100°, etc. Thus 4.4 grams of yellowish gum were recovered. Five-tenths of a gram of this required 29.6 cc. of N/10 sodium hydroxide on titration (the calculated amount for 0.5 gram hexonic acid lactone is 28.07 cc). Consequently, the remainder of the gum was converted into salts in the usual manner by digestion with 10 grams of brucine. Only one crop, 3.2 grams, of crystalline brucine salts melting at 125°–135° could be obtained from these by dissolving in alcohol, even on long standing, leaving a residue of 10.9 grams of gummy salts remaining after distillation under reduced pressure.

Fraction B'.—Five-tenths of a gram of Fraction B' (10.8 grams) required 30 cc. of N/10 sodium hydroxide for neutralization and therefore consisted mainly of hexonic acids. On treatment of the main portion with brucine, 38.3 grams of gummy salts were obtained which, on crystallization, yielded a total of 12.2 grams of crystalline salts melting from 125° to 145°. The remainder, 21.8 grams of gummy salts, was now united with the 10.99 grams of similar salts from C' (see above) and the whole converted by means of barium hydroxide, etc., back into 10 grams of gummy acids which obviously consisted of a mixture of hexonic acids, but which I did not succeed in separating into its components. Treatment with phenylhydrazine gave no crystallizable acid hydrazides.

Fraction A.—The first mentioned ether extract, A, 11.1 grams, was digested for 9 hours in dilute aqueous solution with 50 grams of finely ground strychnine, only 19.5 grams of the alkaloid dissolving. The gummy strychnine salts obtained after distilling off the water at 30 mm. pressure gave, after three crystallizations from absolute alcohol, a total of 17 grams of crude strychnine glycollate melting between 155° and 160°. The noncrystalline and easily soluble strychnine salts left, 18.5 grams, gave back with sodium hydroxide, etc., a total of 6.2 grams of acid gum (alcohol extract). Five-tenths of a gram of this required 39.0 cc. N/10 sodium hydroxide for neutralization (calculated for 1,2-di-

oxybutyrolactone, 42.37 cc.). The remainder gave, on digestion with 19 grams of brucine and subsequent fractional crystallization of the salts obtained, a total of 13.7 grams of brucine salts melting between 180° and 205° . Thirteen grams of easily soluble gummy salts remained which, when treated with barium hydroxide, etc., gave back 1.6 grams of acid gum. This, when converted into the strychnine salt, gave 1.2 grams more of crude strychnine glycollate melting between 150° – 160° , besides 5.8 grams of gummy, easily soluble salts which were united with a corresponding lot from Fraction A' (see below).

Fraction A'.—The second ether-soluble fraction of acid gums, 5.0 grams, took up, on boiling for 9 hours with an excess of strychnine, only 11.0 grams of the alkaloid, and fractional crystallization of the salts obtained gave in all only 2.5 grams of crude glycollic strychnine, melting between 150° and 160° . The remainder, 13.5 grams, was united with a corresponding lot of gummy strychnine salts, 5.8 grams, mentioned above under A. These gave with barium hydroxide, etc., 11.6 grams of strychnine and 5.6 grams of acid gum.

Glycollic Acid from Crude Strychnine Glycollate.—The total amount of crude glycollic strychnine obtained from Fractions A and A' was 20.6 grams; 17.0 grams of this salt gave, with sodium hydroxide, etc., 3.0 grams of syrupy acid (acetic ether extract), and from this by digestion in aqueous solution with an excess of powdered calcium carbonate, etc., 1.9 grams of crystallized calcium glycollate, $\text{Ca}(\text{C}_2\text{H}_3\text{O}_3)_2 \cdot 3\text{H}_2\text{O}$, were obtained. 0.4684 gram of the air-dried salt lost 0.1066 gram of water on drying to constant weight at 120° .

	Calculated for $\text{Ca}(\text{C}_2\text{H}_3\text{O}_3)_2 \cdot 3\text{H}_2\text{O}$.	Found.
H_2O	22.13	22.75

0.7500 gram of the anhydrous calcium salt gave 0.2198 gram of CaO on ignition.

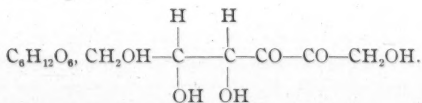
	Calculated for $\text{Ca}(\text{C}_2\text{H}_3\text{O}_3)_2$.	Found.
CaO	29.47	29.32

On the Nature of the Other Crystalline Brucine Salts Obtained.—The total amount of the various crystalline brucine salts (except *d*-mannonic brucine) obtained from the different fractions mentioned above, which had melting points varying from 125° to 205°, was 80.0 grams. These were combined and dissolved in 40 cc. hot water, and, on addition of 235 cc. of alcohol, crystals of a brucine salt melting between 180° and 190°, 21.5 grams in two crops, were obtained. Since this salt gave, on treatment with aqueous barium hydroxide, 15.4 grams of brucine and 4.6 grams of acid gum, the presence of glycerinic acid and of dioxybutyrolactone is probable but not yet established by what I have done.

*A New Hexonic Acid, α -Oxymethyl-*d*-ribonic Acid(?)*.—The alcoholic mother liquors containing still about 56.5 grams of salts were found finally to give, on crystallization from 10 parts of 95 per cent. alcohol, 32.5 grams of transparent flat plates melting from 183° to 186°. These crystals are very sparingly soluble in cold water but dissolve in 10 parts of boiling water and on cooling at least 80 per cent. of the salt separates out in transparent plates. These properties are therefore so striking that this salt can very easily be separated from a mixture. The free acid obtained therefrom by aqueous sodium hydroxide, etc., and subsequent extraction of the salt residue with acetic ether, is a thick gum which gives, with an equal weight of phenylhydrazine in 2 parts of 50 per cent. alcohol, a crystalline phenylhydrazide which, on recrystallization from 50 per cent. aqueous alcohol, melts from 179° to 183°. This hydrazide was fairly difficultly soluble in cold water and practically insoluble in cold alcohol. The specific rotation of the hydrazide in 2 per cent. aqueous solution was found to be +8°.38. 0.4012 gram of the substance and 19.4591 grams of water, $p = 2.020$; $d = 1.004$; found α in a 1 dm. tube = +0°.17. The acid gives apparently an insoluble basic barium salt since it is impossible to obtain it from its brucine salt by the usual method; *i. e.*, treatment with aqueous barium hydroxide. The resulting precipitate contains not only all the brucine, but practically all the acid in the form of an insoluble salt. I lost a considerable quan-

tity of material in this manner. Eleven grams of the brucine salt, when treated with sodium hydroxide, etc., gave 7 grams of brucine and on subsequent extraction of the salt residue with acetic ether 3.1 grams of thick acid gum were obtained. Five-tenths gram of this gum required 28.63 cc. N/10 sodium hydroxide for neutralization, where the calculated amount of N/10 alkali necessary for neutralizing 0.5 gram of a free hexonic lactone is 28.07 cc. These data prove that a hexonic acid must be present which is, however, not identical with any known hexonic acid. The calcium salt, made in the usual way from the acid gum, was found to crystallize from hot, concentrated aqueous solutions in small, translucent cubes which are very sparingly soluble in cold water. It was not analyzed, but gave in one per cent. aqueous solution a specific rotation of $+11^{\circ}.98$; 0.1786 gram substance and 17.6814 grams water, $p = 1.000$, $d = 1.001$, found α in a 1 dm. tube $= +0^{\circ}.12$.

Since Mr. Spoehr, as well as Mr. Rosario,¹ have obtained an analogous new hexonic acid, α -oxymethyl-*d*-arabonic acid—in the oxidation of alkaline solutions of dextrose and laevulose by air as well as by hydrogen peroxide, it is in the highest degree probable that my acid is α -oxymethyl-*d*-ribonic acid, which must be formed from maltose by a preliminary transformation² into dextrose-*d*-glucose which then gives the dextrose glucosone,



This by an asymmetric benzylic acid rearrangement then gives dextrose *d*- α -oxymethylribonic acid.

The alcoholic mother liquors from which the new hexonic acid brucine salt had been removed as thoroughly as possible still contained 25.2 grams gummy brucine salts which could not be obtained in crystalline form. These were, there-

¹ Work soon to be published in THIS JOURNAL.

² Lobry de Bruyn and Ekenstein: Rec. Trav. Chim., 16, 258, 274. Nef: Ann. Chem. (Liebig), 357, 297.

fore, decomposed with barium hydroxide into 16 grams of brucine and 9.0 grams of acid gum, indicating therefore, the presence of other hexonic acids.

Brief Summary of Results of Other Experiments with Maltose and Fehling's Solution.—An experiment with Fehling's solution on 144 grams maltose carried out in practically the same manner as given in detail above gave 133.7 grams of thick, syrupy glucosido acids which on hydrolysis gave 66.7 grams of gummy acids and 55.04 grams of dextrose. Forty-four and seven-tenths grams of the acids dissolved in acetic ether on thorough digestion, leaving, therefore, 22.2 grams of insoluble gum. The ethyl acetate solution deposited on standing 6.5 grams of crystallized mannonic lactone. On treating the gummy acids, 38.2 grams, recovered from the solvent, with 40 cc. alcohol and 38 cc. phenylhydrazine for 24 hours at ordinary room temperature, 9.45 grams of crystalline hexonic acid hydrazides melting from 204° to 206° separated out. On similar treatment with phenylhydrazine the 22.2 grams of gummy acids insoluble in acetic ether gave 25.5 grams of crystalline acid hydrazides. These combined hydrazides, 35 grams, gave on hydrolysis with 7 per cent. sodium hydroxide,¹ 13.05 grams of mannonic lactone, besides 5.5 grams of gummy acids. A portion of the latter when titrated with N/10 alkali gave results agreeing with those calculated for a free hexonic acid, and on converting the main portion of the gum with the calculated amount of brucine into salts (16.8 grams) there were obtained on fractional crystallization from aqueous alcohol 10.0 grams of mannonic brucine and 5.8 grams of the new so-called α -oxymethyl-*d*-ribonic brucine melting at 181° – 183° . This result indicates that *d*-gluconic acid cannot be present in any appreciable quantity. It must, however, be emphasized in this connection that treatment of the various fractions of the acid gums with phenylhydrazine and alcohol never removes the hexonic acids completely in the form of insoluble hydrazides. I obtained, for instance, in working up the acids forming alcohol-soluble hydrazides in the experiment just referred to above

¹ Nef: Ann. Chem. (Liebig), **357**, 225.

(by hydrolysis, etc.), a total of 21.0 grams of the very characteristic α -oxymethyl-*d*-ribonic brucine melting from 181° to 183°.

It is apparent, therefore, that the complete separation of the various hexonic acid hydrazides, which by themselves are practically insoluble in cold or hot absolute alcohol, is prevented to a considerable extent by the presence of the other acids which form alcohol-soluble hydrazides or phenylhydrazine salts.

Summarizing finally, there were obtained from 136.8 grams of anhydrous maltose in the reaction described in detail above 10.6 grams of carbon dioxide, 4.74 grams of formic acid, and 132.8 grams of nonvolatile gums consisting chiefly of glucosido acids. The latter gave on hydrolysis, besides 47.5 grams of dextrose, 82.35 grams of nonvolatile acids. A total of 45.02 grams of these acids was identified quantitatively as follows: 0.35 gram oxalic acid, 3.92 grams glycollic acid, 30.25 grams *d*-mannonic lactone, and 10.5 grams of a new hexonic acid called α -oxymethyl-*d*-ribonic acid. The nature of the remaining 37 grams unidentified acids was not established, mainly because of lack of time.

Experiments with a d-Maltosone and d-Glucosone.—It is extremely probable, from my results with maltose, that only two hexonic acids, namely, *d*-mannonic and α -oxymethyl-*d*-ribonic acid, are obtained in the hydrolysis of the glucosido acids which are formed by the action of Fehling's solution on maltose. In that case, both acids must be formed by an asymmetric benzylic acid rearrangement from 1,2-maltosone and 2,3-maltosone, respectively.¹ 1,2-*d*-Glucosone, which must be the common intermediate product when *d*-glucose, *d*-fructose, and *d*-mannose are oxidized by Fehling's solution, gives, on the other hand, by a partial asymmetric benzylic acid rearrangement, mainly *d*-gluconic acid and only small amounts of *d*-mannonic acid.²

It was, therefore, a point of great interest to prove the correctness of these conclusions by actually studying the

¹ Nef: Ann. Chem. (Liebig), **357**, 281 and 282.

² *Ibid.*, **357**, 284.

behavior of caustic alkalis towards *d*-glucosone as well as *d*-maltosone, substances which are now not so very difficult of access.¹ My preliminary experiments tend to confirm the correctness of the conclusions reached, but I regret to have to admit that the results are not absolutely final or decisive, and can only become so by a very careful repetition of the work with far larger quantities of material.

Experiments with Maltosone.—Maltosone was prepared from the osazone by the method of Emil Fischer and Armstrong.² One hundred and thirty grams of maltose gave, on treatment with aqueous phenylhydrazine acetate, 92.1 grams of maltosazone melting at 210°. On treating this, according to the directions, in 20-gram lots with benzaldehyde, I never obtained more than 11.0 grams of crude maltosone from 45 grams of osazone instead of the calculated 29.4 grams. That this poor yield is due chiefly to an incomplete hydrolysis of maltosazone under the conditions employed by Fischer and Armstrong was proved by subsequent experiments in which an almost quantitative yield was obtained by heating for 10 hours longer and treating a second time, after concentrating the aqueous filtrate to a small volume, with more benzaldehyde. Thus a mixture of 19 grams of maltosazone in 100 parts of boiling water gave finally, after 10 hours' heating on the boiling water bath with 1.5 parts of benzaldehyde, 11.9 grams of crude maltosone, instead of the calculated 12.4 grams. It is, of course, possible that some maltosone had been split into glucosone and dextrose on account of the prolonged heating with boiling water.

The crude maltosone prepared exactly according to Fischer and Armstrong's directions showed the following properties: (a) it gave on treatment in the cold with phenylhydrazine acetate an equal weight of maltosazone, crystallizing in rosettes, melting at 210°, and entirely free from the large, flat, needle-shaped crystals of *d*-glucosazone.³ (b) A solution of 0.2 gram of maltosone in 4 cc. of water, when added to 5 cc. of Fehling's solution, was markedly reduced in one minute, completely

¹ Ber. d. chem. Ges., **35**, 3141.

² Loc. cit.

³ J. Am. Chem. Soc., **25**, 1015. Grimbert: J. Pharm. Chim., **7**, 17-5.

in one-half hour in the cold. If, however, the maltosone was first dissolved in an alkaline tartrate solution, and this mixture allowed to stand 48 hours before the addition of the copper sulphate solution, the same conditions as to concentration and amounts being observed, only slight reduction to cuprous oxide was noticeable, approximately only 8 per cent. of that in the first experiment. (c) Cold solutions of 20 grams of maltosone in 400 cc. of water and of 18.5 grams of crystallized barium hydroxide in 200 cc. of water were mixed and allowed to stand for 48 hours. The calculated amount of sulphuric acid was then added to the dark red solution, which contained also a flocculent precipitate. In order to hydrolyze the supposed dextrose-*d*-mannonic acid formed, the filtrate was then made up to 1 liter with water, 50 grams of sulphuric acid added and the solution boiled five hours. The free sulphuric acid was now removed in the usual manner, care being taken to leave only a trace of barium in the solution. The water was removed by distillation under reduced pressure and the residue, 11.5 grams, was taken up in hot absolute alcohol. On standing, the characteristic crystals, 0.3 gram, of mannonic lactone separated out. These melted, on recrystallization from acetic ether, between 148° – 152° . The rest of the acid gum obtained, 11 grams, was resolved by solution in 20 cc. of alcohol and partial precipitation by addition of 40 cc. ether, into 2 fractions, *i. e.*, 4.8 grams soluble and 6.2 grams insoluble gum. The latter gave, on heating for 8 hours with 19 cc. acetic anhydride at 100° , 10.2 grams of acylated gum of which only 6.8 grams dissolved in hot ether. The latter, on fourfold hydrolysis with five parts of water, finally gave back 4.2 grams of acid gum. Twenty-five hundredths gram of this required 21.1 cc. of N/10 sodium hydroxide for neutralization. The remainder was then converted by means of 13.3 grams brucine into 18.5 grams gummy brucine salts. These gave, on fractional crystallization from alcohol, first 2 grams of crude *d*-mannonic brucine melting from 180° to 190° , which was converted by means of sodium hydroxide into the crystalline lactone melting at 145° – 148° , as well as its phenylhydrazide melting at 200° – 205° , and

second, 1.3 grams melting from 138° to 140° . This, on crystallization from 1.5 cc. water, gave transparent crystalline plates melting between 179° and 180° , and resembling very closely the so-called α -oxymethyl-*d*-ribonic brucine which I obtained from maltose by means of Fehling's solution. Finally, the gummy brucine salts left gave back 2.6 grams of acid gum which, on treatment with phenylhydrazine and alcohol, gave 1.2 grams of crystalline hydrazides melting from 185° to 195° .

Experiment with Glucosone.—Twenty-three and seven-tenths grams of crude maltosone, prepared according to the modified method given above from 38 grams of maltosazone, was hydrolyzed with 5 parts of 5 per cent. sulphuric acid for 5 hours in a boiling water bath. Considerable charring took place in this operation and on freeing the solution, first from sulphuric acid and then from water, 20 grams of a mixture of glucose and glucosone gum were obtained. This gave the following tests: Reduction took place at once with Fehling's solution in the cold. The presence of free glucose was shown by the production of gas with yeast suspension in the fermentation tube, since glucosone does not ferment with yeast.¹ One gram of the gum, when treated with phenylhydrazine acetate, gave rapidly, at room temperature, 0.5 gram of crystalline glucosazone, melting at 205° . The filtrate, on boiling with 0.5 gram of phenylhydrazine and 0.5 cc. of 50 per cent. acetic acid, gave a further crop of *d*-glucosazone, the presence of both 1,2-glucosone and *d*-glucose being thus indicated.² The remaining 18.5 grams of gum was now treated in the cold with one molecule of barium hydroxide, 17.2 grams, and 555 grams of water, giving therefore approximately the same concentration as was employed in the corresponding maltosone experiment described above, and set aside for 24 hours. Darkening and deposition of a flocculent precipitate was noticed and after removal of all but traces of the barium present, the water was distilled off under reduced pressure, a residue of 17.0 grams acid gum being

¹ Fischer and Armstrong: Ber. d. chem. Ges., **35**, 3144.

² E. Fischer: Ber. d. chem. Ges., **23**, 2121.

left. Three and seven-tenths grams of this which dissolved in ether were rejected and the remaining 13.3 grams gum were acylated in the usual manner, 21.8 grams of acylated gums being obtained, of which only 10.6 grams were soluble in hot ether, and fourfold hydrolysis of these with water at 100° gave finally 9.0 grams of acid gum. Five-tenths of a gram of the gum required 32.6 cc. of N/10 sodium hydroxide for neutralization (calculated for pentonic acid lactone, 33.8 cc). The remainder was then converted into brucine salts, which on crystallization by long standing gave finally 12.4 grams of crystalline salts melting from 135° to 145°. These gave back with sodium hydroxide, etc., 2.0 grams of acid gum, of which 0.5 gram, when treated with phenylhydrazine in aqueous alcohol solution, gave 9.5 grams of an acid hydrazide melting from 190° to 195°. The specific rotatory power of this in one per cent. solution was found to be +12°.27; i. e., 0.20 gram substance in 19.8 grams water, $p = 1.0$, $d = 1.002$, found α in 1 dm. tube = +0°.12. This indicates the presence of *d*-gluconic acid since a known sample of *d*-gluconic hydrazide melting at 198° was found to give, in 2 per cent. aqueous solution, $[\alpha]_D^{20} = +13°.0$.

The writer wishes to acknowledge his deep appreciation of the constant help and encouragement from Dr. Nef during the course of the above work.

UREIDES AND CYANAMIDES OF THE OXYFATTY ACIDS.

[SECOND PAPER.]

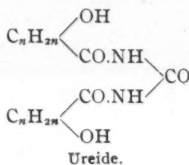
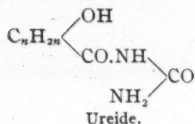
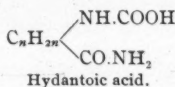
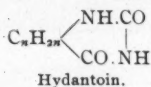
BY ERIK CLEMMENSEN AND ARNOLD H. C. HEITMAN.

In a previous paper¹ we pointed out that the real ureides of the oxyfatty acids, by which we understand urea in which one or more of the hydrogen atoms are replaced by the radicals

$C_nH_{2n} \begin{matrix} \nearrow OH \\ \searrow CO- \end{matrix}$ of the oxyfatty acids up to that time had not been made. In contradistinction to the hydantoin and

¹ THIS JOURNAL, 40, 280.

hydantoic acids these compounds still contain the characteristic alcoholic hydroxyl groups, and their nitrogen atoms are not linked directly to the C_nH_{2n} groups:

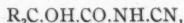


The results obtained in the above mentioned work, in which only the dialkylxyacetic acids were investigated, may be briefly expressed as follows:

By treating the esters of the dialkylxyacetic acids and urea with sodium alcoholate in alcoholic solution dialkylxyacetylureides of the type



are formed, whereas by using thiourea or guanidine instead of urea in the above reaction, dialkylxyacetylcyanamides,

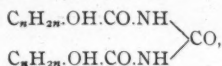


are obtained and not, as would be expected, the thioureides or guaneides. The dialkylxyacetylcyanamides are converted by treatment with acids or alkalies into the dialkylxyacetylureides.

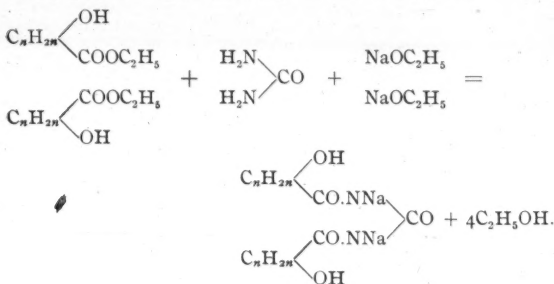
In this paper we have extended our investigation to the lower members of the α -oxyfatty acids, namely glycollic, lactic, α -oxybutyric and α -oxyisovaleric acids, and as we found their behavior in this respect perfectly analogous to that of

the dialkylloxyacetic acids, the results can be expressed in a general way as follows:

The ureides of the α -oxyfatty acids,



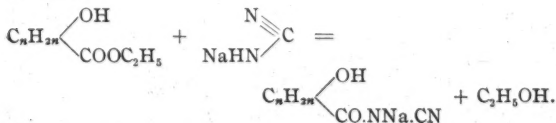
are formed by treating the esters and urea with alcoholic sodium alcoholate, the following reaction taking place:



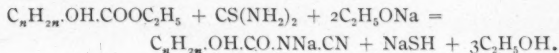
The new ureides are low-melting substances and act as rather strong dibasic acids.

The ureides of the type $\text{C}_n\text{H}_{2n}\text{OH.CO.NH.CO.NH}_2$, corresponding to urea in which only one hydrogen atom is replaced by the group $\text{C}_n\text{H}_{2n}\text{OH.CO}$ —, are not produced by this process.

By treating the esters of the α -oxyfatty acids and thiourea or guanidine with alcoholic sodium alcoholate the cyanamides $\text{C}_n\text{H}_{2n}\text{OH.CO.NH.CN}$ are formed, but not the thioureides or guaneides, as would be expected. In this case the sodium alcoholate apparently converts the thiourea and guanidine into sodium cyanamide, which in turn reacts with the esters as follows:

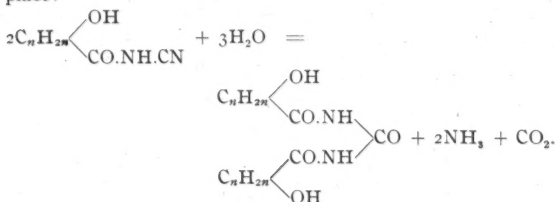


The whole reaction which takes place on treating a mixture of the esters of the α -oxyfatty acids and thiourea with sodium alcoholate is therefore as follows:



The reaction is quite interesting in view of the fact that the malonic esters¹ and the alkyl substituted malonic esters² under the same conditions yield the thioureides and guaneides, and seems to be typical for the α -oxyfatty acids.

The new cyanamides are high-melting, well crystallizing substances, which on boiling with dilute acids (for instance, 10 per cent. sulphuric acid) are quantitatively converted into the above mentioned ureides, the following reaction taking place:



Some interesting by-products are obtained by the action of sodium alcoholate on the esters and thiourea, as small quantities of thiocyanates of the α -oxyfatty acids, $\text{C}_n\text{H}_{2n}\text{OH.CO.S.CN}$, always seem to be formed.

Now acyl thiocyanates apparently have not been made before. Dixon and Doran have shown³ that lead thiocyanate, when treated with acid chlorides, yields acyl thiocarbimides R.CO.NCS and not the acyl thiocyanates R.CO.S.CN , as would be expected, and that Michael's acetyl and butyryl thiocyanate⁴ really are the isomeric thiocarbimides. Dixon, therefore, concludes that acyl thiocyanates are not yet known.⁵

¹ Michael: *J. prakt. Chem.*, [2] **35**, 456.

² Fischer and Diltz: *Ann. Chem. (Liebig)*, **335**, 334.

³ *J. Chem. Soc.*, **67**, 575.

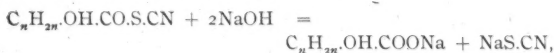
⁴ *Ann. Chim. Phys.*, [5] **11**, 295, 300.

⁵ *J. Chem. Soc.*, **93**, 684.

The acyl thiocarbimides are pungent, very reactive liquids which are immediately decomposed by cold water and some of which are so unstable that all efforts to isolate them have been in vain.

Now the compounds obtained by us in the above mentioned process have quite other properties, as they are stable, crystalline substances, which can be boiled with water and dilute acids without decomposition.

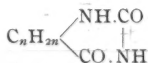
It is therefore out of question to regard them as acyl thiocarbimides, and as they have the right empirical formula, and on boiling with alkali hydroxides yield salts of thiocyanic acid and of the oxyfatty acids,



there is every reason to consider them as thiocyanates of these acids.

They thus represent the first known acyl thiocyanates and we therefore have decided to make a closer investigation of them, possibly including some of the other fatty acids, and to publish the results in a later paper.

In the literature and text-books it is a common mistake to designate the compounds having the formula

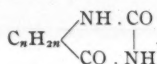


as ureides of the oxyfatty acids although they lack the presence

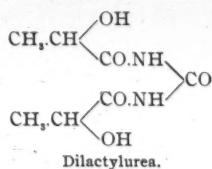
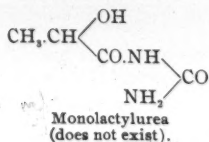
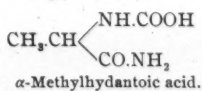
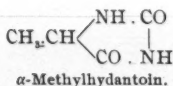
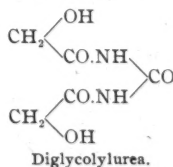
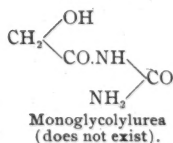
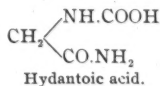
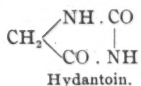
of the radical $\text{C}_n\text{H}_{2n} \begin{cases} \text{OH} \\ \text{CO—} \end{cases}$ which certainly should be a necessary requirement for these compounds and we have, strange to say, not been able to find any contradiction to this nomenclature, although the ureides almost everywhere clearly are defined as substitution products of urea with acid radicals.

For instance the compound $\text{CH}_2 \begin{cases} \text{NH.CO} \\ \text{CO.NH} \end{cases}$ is called glycolylurea notwithstanding that it does not contain the glycolyl

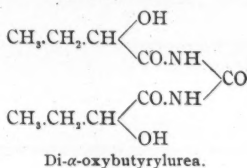
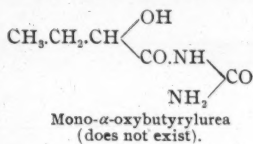
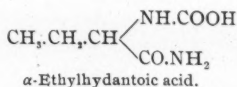
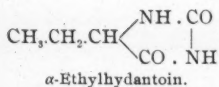
(oxyacetyl) group $\text{CH}_2 \begin{matrix} \text{OH} \\ \diagup \\ \text{CO} \end{matrix}$, for to follow Dixon¹ and call the group $\text{—CH}_2\text{CO—}$ glycolyl would certainly be contrary to all established rules of nomenclature. It would be more consistent to reserve the term ureides of the oxyfatty acids for ureas containing the group $\text{C}_n\text{H}_{2n} \begin{matrix} \text{OH} \\ \diagup \\ \text{CO} \end{matrix}$ and retain the name hydantoin for those with the formula



The nomenclature of the first members of these series would therefore be as follows:



¹ J. Chem. Soc., 71, 637.



We had considerable trouble in preparing the esters of the α -oxyfatty acids in sufficient quantities, as the different methods described in the literature gave very unsatisfactory yields, until a paper on esterification by Bogojawlensky and Narbutt¹ helped us to overcome our difficulties. They recommend that esterifications be carried out by boiling the acids and alcohols with anhydrous copper sulphate, and have applied this method to a large number of acids with excellent results. By dehydrating the copper sulphate a small quantity of sulphuric acid anhydride is formed, and this seems to accelerate the esterification, and they further show that the yield of esters in many cases can be improved by adding small amounts of sulphuric acid.

In order to determine whether this method was suitable for preparing the esters of the α -oxyfatty acids (Bogojawlensky and Narbutt have tried it only on acids which can be esterified with sulphuric or hydrochloric acid) we boiled the respective acids, dissolved in excess of absolute alcohol, with anhydrous copper sulphate with and without an addition of sulphuric acid. The results were however not good, as the sulphuric acid decomposed in great part the esters formed, when we tried to distil them off.

It was only when no sulphuric acid was used and the copper sulphate was dehydrated at so low a temperature that no decomposition took place, that we obtained good yields of the esters. The operation was carried out as follows:

¹ Ber. d. chem. Ges., 88, 3344.

The dried acid was dissolved in commercial absolute alcohol and boiled with anhydrous copper sulphate for about 24 hours. In dehydrating the copper sulphate care must be taken to do it at as low temperature as possible, so that no decomposition, with formation of sulphuric acid anhydride, takes place. The reaction product was then filtered, the alcohol distilled off and the ester rectified.

The yield was good for all four acids, and the method seems to be especially adapted to the preparation of esters easily decomposed by water, which is the case with most of the esters of the oxyfatty acids, and to be able to displace the more or less tedious processes now in use for the preparation of these esters.

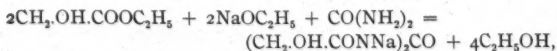
Thus the operations consisting in (1) heating the potassium or silver salts with alkyl iodides, (2) heating the halogen substituted fatty acids with sodium acetate and absolute alcohol, and (3) heating the anhydrides with absolute alcohol all require to be carried out under pressure, while another method much used, distillation of the calcium salts with potassium alkyl sulphate, gives very unsatisfactory yields.

EXPERIMENTAL.

Diglycolylurea, $\begin{matrix} \text{CH}_2\text{OH.CO.NH} \\ \text{CH}_2\text{OH.CO.NH} \end{matrix} \text{CO.}$ —The ethyl glycollate

was made by boiling 100 grams glycollic acid and 200 grams commercial absolute alcohol with 75 grams anhydrous copper sulphate for 24 hours. The copper sulphate was then filtered off, and the ester rectified; yield, 95 grams ester boiling at 158°–160°.

In order to make the glycolylurea, 3 grams sodium were dissolved in 100 cc. absolute alcohol, and to the cooled solution were added 8 grams urea and 20.8 grams ethyl glycollate. The calculated amount of sodium, corresponding to two atoms sodium for two molecules ester, is 4.6 grams,



but it was found that the smaller amount of sodium gave better results.

The whole was boiled in a flask with return condenser for two hours. Most of the alcohol was then distilled off, the remainder containing the sodium salt of the glycolylurea allowed to cool and carefully acidified with dilute acetic acid (10 per cent.). The rest of the alcohol was then distilled off and the remaining liquid extracted with ether several times. After evaporation of the ether the ureide remained as an oil, which on standing a short time solidified to a radiated crystalline mass. The substance was dissolved in boiling benzene, from which it crystallized in colorless, very irregular, thin plates melting at 88° – 89° and this melting point was not changed by a further recrystallization. The yield was 7 grams or about 40 per cent. of the theoretical.

0.2599 gram substance gave 0.3301 gram CO_2 and 0.0985 gram H_2O .

0.2956 gram substance gave 43.5 cc. N at 25° and 741 mm.

	Calculated for $\text{C}_5\text{H}_8\text{O}_5\text{N}_2$	Found.
C	34.07	34.64
H	4.58	4.22
N	15.91	15.99

Diglycolylurea can also be made by boiling glycolylcyanamide (see below) with dilute sulphuric acid.

Five grams glycolylcyanamide were boiled for fifteen minutes with 100 cc. dilute sulphuric acid (10 per cent.) and the ureide formed shaken out with ether several times. After evaporation of the ether a colorless oil remained which on standing solidified to a white radiated crystalline mass weighing 4.1 grams, which is about 93 per cent. of the theoretical. Crystallized from boiling benzene it melted at 88° .

Diglycolylurea is very easily soluble in water, alcohol, ether and chloroform, slightly soluble in cold benzene, more so in warm benzene and nearly insoluble in petroleum ether. Carefully heated in a test tube it boils without decomposition, condensing further up in the tube in the form of a liquid, which on cooling solidifies to a crystalline mass. It is not

decomposed by boiling carbonates and dilute acids but decomposition takes place, with evolution of ammonia, on boiling with alkali hydroxides even in very dilute solution. It acts as a quite strong dibasic acid, which even in the cold decomposes the alkali, and the alkali-earth carbonates, forming very soluble salts.

The silver salt is best prepared by precipitating a solution of alkali ureide with silver nitrate. Recrystallized from boiling water it forms long silky needles. It is almost insoluble in cold water and alcohol, more soluble in boiling alcohol, from which it crystallizes in long monoclinic prisms, and quite readily soluble in warm water.

Air-dried, it contains 2.5 molecules water of crystallization, which it does not lose *in vacuo* over sulphuric acid.

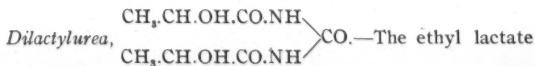
0.2978 gram substance gave 0.1479 gram Ag.

	Calculated for $C_8H_6O_5N_2Ag_3 \cdot 2.5H_2O$.	Found.
Ag	49.61	49.67

At 100° the salt loses one molecule water.

0.2455 gram substance gave 0.1273 gram Ag.

	Calculated for $C_8H_6O_5N_2Ag_3 \cdot 1.5H_2O$.	Found.
Ag	51.76	51.85



was made as follows: One hundred grams lactic acid (75 per cent.) were dried on the steam bath for 48 hours, then mixed with 200 cc. commercial absolute alcohol and 75 grams anhydrous copper sulphate and boiled for 24 hours. The rectified ester boiled at 153°–155°. Yield, 70 grams. Three grams sodium were dissolved in 100 cc. absolute alcohol and to the cooled solution were added 8 grams urea and 23.6 grams ethyl lactate and the whole boiled for two hours. The reaction product was freed from most of the alcohol, then cooled, carefully acidified with dilute acetic acid (10 per cent.) and, after the rest of the alcohol had been distilled off, extracted with ether several times. After evaporation of the ether the

dilactylurea remained as an almost colorless oil. On standing *in vacuo* over sulphuric acid it slowly solidified to a somewhat soft, crystalline mass. Sometimes it would not crystallize at all even on standing for weeks but crystallization could always be effected by contact with a crystal already formed.

The substance no doubt contained impurities, especially lactic acid, and as we were not able to crystallize it from any solvent, we tried to purify it through one of the salts. By investigating these we found that the ureide on boiling with zinc oxide yields a zinc salt which is practically insoluble in boiling water, and as zinc lactate is easily soluble in warm water, this salt is well adapted for purifying the substance. The ureide was therefore dissolved in water, the solution boiled with an excess of zinc oxide, and the precipitated zinc salt collected and washed thoroughly with hot water. It was then dissolved in dilute sulphuric acid (25 per cent.), and the solution extracted several times with ether. After evaporation of the ether, the ureide remained as a colorless oil, which on standing solidified to a crystalline mass of small needles, appearing under the microscope as pointed rhombic prisms. When heated the ureide begins to soften at 47° and melts at 49° – 50° .

0.3361 gram substance gave 0.5033 gram CO_2 and 0.1690 gram H_2O .

0.2919 gram substance gave 36.3 cc. N at 25° and 746 mm.

	Calculated for $\text{C}_7\text{H}_{13}\text{O}_5\text{N}_2$	Found.
C	41.15	40.84
H	5.93	5.60
N	13.73	13.61

Dilactylurea may also be made by boiling lactylcyanamide (see below) with dilute sulphuric acid. Five grams lactylcyanamide were boiled for fifteen minutes with 100 cc. sulphuric acid (10 per cent.) and the cooled solution extracted with ether. The ureide was then obtained as a colorless oil which on standing solidified to a crystalline mass of small needles. It began to soften at 47° and melted at 49° – 50° . The yield was 4.2 grams, which is practically the theoretical.

Dilactylurea is very easily soluble in water, alcohol, ether and chloroform, quite readily soluble in boiling benzene, from which it separates as an oil on cooling, and nearly insoluble in petroleum ether. It is not decomposed by boiling with alkali carbonates or dilute acids but on warming with alkali hydroxides ammonia is given off. When the substance is carefully heated in a test tube it boils without decomposition. Like glycolylurea it acts as a dibasic acid, which even in the cold acts on the alkali and alkali-earth carbonates, forming very soluble salts.

When copper chloride is added to an excess of concentrated solutions of calcium, barium, strontium or magnesium salts of lactylurea, double salts of the formula $C_{14}H_{20}O_{10}N_4CuM$ ($M = Ca, Ba, Sr$ or Mg) are precipitated as ultramarine-blue bodies, which are slightly soluble in water and insoluble in alcohol. They are readily soluble in excess of copper chloride and on boiling these solutions bright green precipitates of basic copper salts are formed.

For analysis the calcium copper salt was dried at 100° .

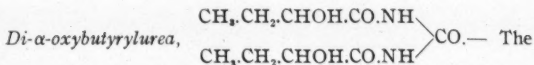
1.1840 gram substance gave 0.1833 gram Cu_2S and 0.1290 gram CaO .

	Calculated for $C_{14}H_{20}O_{10}N_4CaCu$.	Found.
Cu	12.52	12.36
Ca	7.90	7.78

The silver salt is obtained in the same way as silver glycolylurea and crystallizes from warm water in groups of small needles which under the microscope appear as monoclinic prisms. It is very sparingly soluble in cold water and alcohol, slightly soluble in boiling alcohol, and quite readily soluble in warm water. Dried in the air or *in vacuo* over sulphuric acid it contains 1.5 molecules water of crystallization, which it does not lose at 100° .

0.2050 gram substance gave 0.0996 gram Ag.

	Calculated for $C_7H_{10}O_2N_2Ag \cdot 1.5H_2O$.	Found.
Ag	48.50	48.59



ethyl α -oxybutyrate we used was made by boiling 100 grams α -oxybutyric acid and 200 cc. commercial absolute alcohol with 75 grams anhydrous copper sulphate for 12 hours. The average yield of ester was 95 grams. Boiling point, 165°.

In preparing the α -oxybutyric acid we used the method of Markownikow¹ as modified by Bischoff and Walden,² which consists in boiling α -brombutyric acid with potassium carbonate. The α -brombutyric acid was made by brominating butyric acid according to the directions of Genvesse.³

The ureide was made in the usual way. Four grams sodium were dissolved in 100 cc. absolute alcohol and to the cooled solution were added 8 grams urea and 26.4 grams ethyl α -oxybutyrate and the whole boiled for three hours. Most of the alcohol was then distilled off, the remainder acidified with dilute acetic acid (10 per cent.), the rest of the alcohol distilled off, and the ureide shaken out with ether. The ether solution yielded on evaporation a faintly yellow oil, which *in vacuo* over sulphuric acid solidified to a crystalline mass. The yield was 17 grams impure ureide, which is about 73 per cent. of the theoretical.

As we did not succeed in crystallizing the substance from a solvent, it was purified through the silver salt. The ureide was dissolved in the equivalent amount of sodium carbonate and precipitated with silver nitrate. The silver salt was washed with water, recrystallized from boiling water and decomposed with hydrogen sulphide. The filtrate from the silver sulphide was extracted with ether, and the ether evaporated, whereupon the ureide remained as a colorless oil, which on standing solidified to a mass of short prismatic crystals. Under the microscope they appeared as stout, rhombic prisms. The ureide melts at 48°–49° and begins to soften at 46°.

¹ Ann. Chem. (Liebig), 153, 242.

² *Ibid.*, 279, 104.

³ Bull. Soc. Chim., [3] 7, 364.

0.2291 gram substance gave 0.3904 gram CO_2 and 0.1351 gram H_2O .

0.2089 gram substance gave 22.8 cc. N at 27° and 745 mm.

	Calculated for $\text{C}_9\text{H}_{16}\text{O}_5\text{N}_4$	Found.
C	46.52	46.47
H	6.95	6.57
N	12.07	11.80

Di- α -oxybutyrylurea can also be made by boiling α -oxybutyrylcyanamide (see below) with dilute sulphuric acid. Five grams oxybutyrylcyanamide were boiled with 100 cc. sulphuric acid (10 per cent.) for fifteen minutes and the ureide shaken out with ether. It was then obtained as a colorless oil which on standing solidified to a mass of stout rhombic prisms melting at 48° - 49° . The yield was practically the theoretical.

Di- α -oxybutyrylurea is easily soluble in water, alcohol and ether, quite readily soluble in benzene and almost insoluble in petroleum ether. It is not decomposed on boiling with carbonates and dilute acids, but decomposition takes place on warming with alkali hydrates with evolution of ammonia.

Like the other ureides of this class it acts as a quite strong dibasic acid, yielding soluble salts with alkali and alkali-earth carbonates.

Solutions of calcium, barium, strontium and magnesium salts of the ureide give with copper chloride precipitates of the characteristic blue double salts of the formula $\text{C}_9\text{H}_{16}\text{O}_5\text{N}_4\text{CuM}$, which are but slightly soluble in water and dissolve in excess of copper chloride.

The silver salt is obtained in the usual way and crystallizes from warm water in groups of small monoclinic needles. Dried in the air and *in vacuo* over sulphuric acid it contains 1.5 molecules water of crystallization, which it does not lose at 100° .

0.2178 gram substance gave 0.0990 gram Ag.

	Calculated for $\text{C}_9\text{H}_{14}\text{O}_5\text{N}_4\text{Ag}_2 \cdot 1.5\text{H}_2\text{O}$	Found.
Ag	45.62	45.46

Di- α -oxyisovalerylurea, $\begin{matrix} (\text{CH}_3)_2\text{CH.CHOH.CO.NH} \\ (\text{CH}_3)_2\text{CH.CHOH.CO.NH} \end{matrix} \text{CO}$, was

made as follows: Four grams sodium were dissolved in 100 cc. absolute alcohol and boiled with 8 grams urea and 29.2 grams ethyl α -oxyisovalerate for three hours. Most of the alcohol was then distilled off and the remaining liquid acidified with acetic acid (10 per cent.). After evaporation of the rest of the alcohol the ureide on cooling separated out as an oil. It was redissolved in boiling water and then obtained as a colorless oil boiling at 277° – 279° at ordinary pressure, and having a specific gravity at 15° of 1.1922. The yield was 22 grams, which is about 85 per cent. of the theoretical.

0.2304 gram substance gave 0.4239 gram CO_2 and 0.1523 gram H_2O .

0.1823 gram substance gave 18.2 cc. N at 26° and 746 mm.

	Calculated for $\text{C}_{11}\text{H}_{20}\text{O}_5\text{N}_2$	Found.
C	50.73	50.18
H	7.75	7.36
N	10.77	10.87

Di- α -oxyisovalerylurea can also be made by treating α -oxyisovalerylcyanamide (see below) with dilute sulphuric acid. Five grams oxyisovalerylcyanamide were boiled with 100 cc. sulphuric acid (10 per cent.) for half an hour and the solution extracted with ether. After evaporation of the ether the ureide remained as a colorless oil which could not be brought to crystallization even on standing for weeks *in vacuo* over sulphuric acid. The yield was practically quantitative.

0.1531 gram substance gave 0.2825 gram CO_2 and 0.1019 gram H_2O .

0.1215 gram substance gave 12.2 cc. N at 26° and 746 mm.

	Calculated for $\text{C}_{11}\text{H}_{20}\text{O}_5\text{N}_2$	Found.
C	50.73	50.32
H	7.75	7.42
N	10.77	10.93

The ureide is sparingly soluble in cold water, readily soluble in warm water and very easily soluble in alcohol and ether.

It dissolves quite readily in benzene and only slightly in petroleum ether. It dissolves easily in alkali carbonates and is precipitated from these solutions on addition of acids. It is decomposed on boiling with alkali hydrates even in very dilute solution, but it can be boiled with dilute acids and alkali carbonates without decomposition. The double salts $C_{22}H_{36}O_{10}N_4CuM$ (where $M = Ca, Ba, Sr$ or Mg) are made by boiling the ureide with excess of the alkali-earth carbonates and precipitating from the concentrated filtrate with copper chloride. They are then obtained as ultramarine-blue substances which are almost insoluble in water and readily dissolve in excess of copper chloride.

For analysis the calcium copper salt was dried at 100° .

0.9975 gram substance gave 0.1285 gram Cu_2S and 0.0891 gram CaO .

	Calculated for $C_{22}H_{36}O_{10}N_4CaCu$.	Found.
Cu	10.25	10.28
Ca	6.47	6.38

The silver salt can be made by precipitating a solution of alkali ureide with silver nitrate. Recrystallized from boiling water it forms small slender monoclinic needles. It is slightly soluble in cold water, much more so in warm water and dissolves readily in cold alcohol.

Air-dried the salt contains 2.5 molecules water of crystallization.

0.2703 gram substance gave 0.1120 gram Ag .

	Calculated for $C_{11}H_{18}O_5N_2Ag_2 \cdot 2.5H_2O$.	Found.
Ag	41.58	41.44

On standing *in vacuo* over sulphuric acid this salt loses one molecule water of crystallization and the remaining 1.5 molecules are retained at 100° .

0.2993 gram substance gave 0.1291 gram Ag .

	Calculated for $C_{11}H_{18}O_5N_2Ag_2 \cdot 1.5H_2O$.	Found.
Ag	43.07	43.13

The ethyl α -oxyisovalerate we used was made in our usual way by boiling 100 grams α -oxyisovaleric acid and 200 cc. absolute alcohol with 50 grams anhydrous copper sulphate for 12 hours. The yield was about 100 grams. The rectified ester boiled at 174° – 176° .

The α -oxyisovaleric acid was made from α -bromisovaleric acid by the same method we used for making α -oxybutyric acid.

Cyanamides of the α -Oxyfatty Acids, $C_nH_{2n}.OH.CO.NH.CN$.—

As already mentioned, these compounds were obtained by a process which we expected would yield the thioureides,



namely, by heating the esters of the α -oxyfatty acids and thiourea with alcoholic sodium alcoholate.

Glycolylcyanamide, $CH_2.OH.CO.NH.CN$, was made as follows: Two grams sodium were dissolved in 100 cc. absolute alcohol and to the cooled solution were added 9 grams thiourea and 10.4 grams ethyl glycollate. The whole was boiled for one hour. Most of the alcohol was then distilled off, and to the cooled remainder was added exactly as much dilute acetic acid (20 per cent.) as was necessary to bind all the sodium. On standing in a cool place the glycolylcyanamide crystallized out. It was washed with alcohol and dissolved in boiling alcohol, from which it crystallized in large shining monoclinic prisms. The yield was 6 grams, which is 60 per cent. of the theoretical. On being heated it began to decompose at 217° and was entirely melted at 237° .

0.3386 gram substance gave 0.4487 gram CO_2 and 0.1247 gram H_2O .

0.2308 gram substance gave 60.2 cc. N at 27° and 740 mm.

	Calculated for $C_2H_4O_2N_2$	Found.
C	35.98	36.14
H	4.03	4.10
N	28.01	28.00

Glycolylcyanamide is quite readily soluble in cold water, less so in cold alcohol. It dissolves readily in warm alcohol and very easily in warm water. It is almost insoluble in ether, benzene and petroleum ether. It dissolves easily in cold alkali hydroxides and is precipitated on addition of acids if the solutions are concentrated enough, but redissolves in excess of these. On boiling with acids (for instance, 10 per cent. sulphuric acid) it is quantitatively converted into diglycolylurea. The same transformation no doubt at first takes place on boiling with alkali hydroxides, but in this case the ureide formed is also decomposed.

Glycolyl Thiocyanate, $\text{CH}_2\text{OH.CO.S.CN}$.—The mother liquid from the glycolylcyanamide was extracted with ether several times, and the ether evaporated. A yellow oil remained, in which, on standing *in vacuo* over sulphuric acid, some long needles crystallized out. Dry ether dissolved the oil, while the needles remained undissolved. They were recrystallized from a little warm water and then obtained as stout short prisms melting at 171° – 172° . After being melted the substance gave with ferric chloride the deep red color characteristic for rhodanates. It was thus nothing but thiourea. The oil was freed from ether. On standing it solidified to a yellow crystalline mass, which was dissolved in a large amount of boiling benzene. On cooling, the solution deposited a little thiourea. It was filtered and concentrated, whereupon a substance crystallized out in groups of small slender yellow needles. Once more recrystallized from boiling benzene, it melted constant at 106° .

The substance contained sulphur. Its aqueous solution was not colored red by ferric chloride, but after being boiled with sodium hydroxide and then carefully acidified, a deep red color was produced by addition of ferric chloride. When the substance was boiled with sodium hydroxide, acidified and then extracted with ether an oil was obtained, which was identified as glycollic acid. These reactions would indicate that the substance was glycolyl thiocyanate, $\text{CH}_2\text{OH.CO.S.CN}$, and a nitrogen and sulphur determination confirmed

this assumption, although we had not enough material to make a complete analysis.

0.0682 gram substance gave 7.7 cc. N at 28° and 750 mm.

0.0890 gram substance gave 0.1770 gram BaSO₄.

	Calculated for C ₃ H ₅ O ₂ N ₂ S.	Found.
N	11.96	12.22
S	27.39	27.34

Glycolyl thiocyanate is easily soluble in water, alcohol and ether, readily soluble in warm benzene, less so in cold, and nearly insoluble in petroleum ether.

Lactylcyanamide, CH₃.CH.OH.CO.NH.CN. — Unlike the other cyanamides of this class this compound is already known, as it was obtained by Merting¹ by adding lactide to a concentrated alcoholic solution of potassium cyanamide.

We made it in the following way: Two grams sodium in 100 cc. absolute alcohol were boiled for one hour with 9 grams thiourea and 11.8 grams ethyl lactate. Most of the alcohol was then distilled off and to the cooled residue was added exactly as much acetic acid (20 per cent.) as was necessary to bind all the sodium. On standing, the lactylcyanamide crystallized out. It was recrystallized from boiling alcohol, from which it separated out in groups of small flat needles. The yield was 8 grams, which is about 70 per cent. of the theoretical. The substance begins to soften at 208° and melts at 212°.

0.1362 gram substance gave 0.2103 gram CO₂ and 0.0619 gram H₂O.

0.0915 gram substance gave 21.0 cc. N at 28° and 746 mm.

	Calculated for C ₄ H ₅ O ₂ N ₂ .	Found.
C	42.08	42.11
H	5.30	5.06
N	24.56	24.71

Lactylcyanamide is quite readily soluble in cold water, much less so in cold alcohol. It dissolves readily in boiling alcohol and still more easily in warm water from which it

¹ J. prakt. Chem., [2] 17, 31.

crystallizes in plates in groups resembling cauliflower. It is nearly insoluble in ether, benzene and petroleum ether. It dissolves very easily in cold alkali hydroxides and is precipitated on adding acids if the solutions are not too dilute, but redissolves in excess of these. On boiling with acids (for instance 10 per cent. sulphuric acid) it is quantitatively converted into dilactylurea.

Lactyl Thiocyanate, $\text{CH}_3\text{CH.OH.CO.S.CN}$.—The mother liquid from the lactylcyanamide, which contained small quantities of lactyl thiocyanate, was extracted with ether several times and the ether evaporated. A yellow oil was obtained which on standing solidified to a crystalline mass. This was dissolved in anhydrous ether, whereby a little thiourea was left undissolved, the ether evaporated and the residue dissolved in boiling benzene. On standing, the substance crystallized out in groups of small colorless needles. Recrystallized again from benzene it melted constant at $89^\circ\text{--}90^\circ$.

0.1834 gram substance gave 0.2437 gram CO_2 and 0.0595 gram H_2O .

0.1668 gram substance gave 16.6 cc. N at 27° and 737 mm.

0.1058 gram substance gave 0.1902 gram BaSO_4 .

	Calculated for $\text{C}_4\text{H}_5\text{O}_2\text{NS}$.	Found.
C	36.61	36.24
H	3.84	3.61
N	10.68	10.64
S	24.46	24.71

Lactyl thiocyanate is easily soluble in water, alcohol and ether, only sparingly soluble in cold benzene, more so in boiling benzene and almost insoluble in petroleum ether. Its aqueous solution is not colored red by ferric chloride even after boiling with dilute acids but on warming with alkali hydroxides it is decomposed into thiocyanic acid and lactic acid.

As already mentioned these thiocyanates represent the first known acyl thiocyanates, and we will therefore return to them in a later paper in which will be included the α -oxybutyryl and α -oxyisovaleryl thiocyanates.

α -Oxybutyrylcyanamide, $\text{CH}_3\text{CH}_2\text{CHOH.CO.NH.CN}$, was

made as follows: Two and two-tenths grams sodium were dissolved in 100 cc. absolute alcohol and to the cooled solution were added 9 grams thiourea and 13.2 grams ethyl α -oxybutyrate and the whole boiled for one hour. The alcohol was then distilled off as completely as possible and to the cooled residue was added just enough acetic acid (10 per cent.) to combine with all the sodium. On standing, the α -oxybutyrylcyanamide separated out. It was washed with a little cold water and dissolved in boiling water, from which it crystallized in groups of thin shining plates. The yield was 9 grams, which is about 70 per cent. of the theoretical. The substance began to soften at 205° and melted at 207° - 208° .

0.1689 gram substance gave 0.2907 gram CO_2 and 0.0930 gram H_2O .

0.1612 gram substance gave 32.8 cc. N at 26° and 736 mm.

	Calculated for $\text{C}_5\text{H}_9\text{O}_3\text{N}_3$	Found.
C	46.84	46.94
H	6.30	6.13
N	21.88	21.84

α -Oxybutyrylcyanamide is only slightly soluble in cold water, more so in hot water, from which it crystallizes in plates. It is quite readily soluble in cold alcohol and easily soluble in boiling alcohol, crystallizing from this in needles which under the microscope appear as slender monoclinic prisms. It is sparingly soluble in warm chloroform, crystallizing on cooling in silky needles, and nearly insoluble in ether, benzene and petroleum ether.

It dissolves easily in cold alkali hydroxides, is precipitated from these solutions on addition of acids but redissolves in excess of these.

When boiled with acids (10 per cent. sulphuric acid) it is quantitatively converted into di- α -oxybutyrylurea.

α -Oxyisovalerylcyanamide, $(\text{CH}_3)_2\text{CH}.\text{CHOH}.\text{CO}.\text{NH}.\text{CN}$, was made in a similar way as the oxybutyryl compound, namely, by boiling 2.4 grams sodium in 100 cc. absolute alcohol with 9 grams thiourea and 14.6 grams ethyl α -oxyisovalerate for one hour. The alcohol was then distilled off as completely

as possible and acetic acid (10 per cent.) added in the usual way, whereupon the α -oxyisovalerylcyanamide separated out. It was washed with cold water and dissolved in boiling water, from which it crystallized in groups of very irregular flat needles apparently monoclinic. The yield was 11 grams, or about 77 per cent. of the theoretical. The substance began to soften at 216° and melted at 219° .

0.2269 gram substance gave 0.4182 gram CO_2 and 0.1434 gram H_2O .

0.1684 gram substance gave 31.0 cc. N at 25° and 738 mm.

	Calculated for $\text{C}_6\text{H}_{10}\text{O}_2\text{N}_2$	Found.
C	50.67	50.27
H	7.09	7.04
N	19.72	19.92

α -Oxyisovalerylcyanamide is only slightly soluble in cold water, readily soluble in boiling water. It is quite readily soluble in cold alcohol and easily soluble in warm alcohol, from which it crystallizes in small needles appearing under the microscope as long slender monoclinic prisms. It is almost insoluble in ether, chloroform and benzene.

It dissolves very easily in cold caustic alkalies, is precipitated from these solutions on addition of acids, but redissolves in excess of these.

Like the other cyanamides of this class it is quantitatively converted into di- α -oxyisovalerylurea on boiling with 10 per cent. sulphuric acid.

LABORATORIES OF PARKE, DAVIS AND CO.,
June, 1909.

[Contributions from the Sheffield Laboratory of Yale University.]

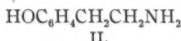
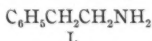
CLXX.—RESEARCHES ON AMINES: SYNTHESIS OF METHYLPHENYLETHYLAMINE.

[FIRST PAPER.]

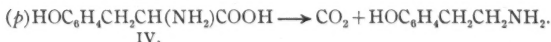
BY TREAT B. JOHNSON AND HERBERT H. GUEST.

The progress of physiological research in recent years has demonstrated the importance of a thorough chemical in-

vestigation of the bases phenylethylamine and *p*-oxyphenylethylamine. Results have been obtained which show that these bases, and several of their derivatives, occupy a prominent position among the aromatic compounds which are found among the decomposition products of proteins. Notwithstanding the fact that it has been known for a long time that they are formed in digestion and metabolism, yet our knowledge of them is extremely meagre. This paper may therefore be considered as a preliminary contribution to the study of substitution products of phenylethylamine (I) and *p*-oxyphenylethylamine (II):



These two bases have been obtained as cleavage products in protein metabolism and are formed from the amino acids phenylalanine (III) and tyrosine (IV), respectively, by the action of specific enzymes:



Gautier and Étard¹ observed that phenylethylamine is formed, with other bases, by the putrefaction of fish flesh (mackerel), but assigned to it the incorrect formula $\text{C}_8\text{H}_{13}\text{N}$. Nencki² and later Spiro³ obtained it among the decomposition products of gelatin after putrefaction with pancreas, and isolated it in the form of its platinum chloride double salt and its benzoyl derivative. It is interesting to note here that O. de Coninck⁴ obtained a base having the empirical composition $\text{C}_8\text{H}_{11}\text{N}$ by putrefaction of the flesh of cuttle fish, with the sepia bags removed. An amine having this same composition was also obtained by Emmerling⁵ by the action of bacteria (*streptococci*) on fibrin from swine blood.

¹ Compt. Rend., **94**, 1601.

² Nencki's Opera Omnia, **1**, 195; **2**, 171; J. prakt. Chem., **26**, 47; Monats. Chem., **10**, 506; Sitzun. Wien., **1889**, 10.

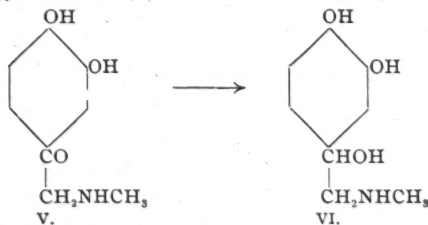
³ Beitr. chem. Physiol. (Hofmeister), **1**, 347.

⁴ Compt. Rend., **106**, 858, 1604.

⁵ Ber. d. chem. Ges., **30**, 1863.

Emerson¹ discovered *p*-oxyphenylethylamine among the products of autodigestion of beef pancreas and later Langstein² identified the base as one of the cleavage products in peptic digestion of ovalbumin. Van Slyke and Hart³ found the base among the proteolytic end-products formed during the ripening of Cheddar cheese and later Winterstein and Küng⁴ observed that it is also a normal constituent of Emmentaler cheese. Barger and Walpole⁵ isolated the base from putrid meat and recently Barger⁶ has found that it is one of the active principles of ergot.

An important derivative of *p*-oxyphenylethylamine is adrenaline (suprarenine, epinephrine), the principle of the suprarenal glands which raises the blood pressure.⁷ This has been isolated,⁸ synthesized and shown to be identical with the amino alcohol⁹ (VI), obtained by reduction of methylaminoacetopyrocatechol¹⁰ (V):



¹ Beitr. chem. Physiol. (Hofmeister), **1**, 501.

² *Ibid.*, **1**, 507; **2**, 229.

³ THIS JOURNAL, **30**, 8.

⁴ Z. physiol. Chem., **59**, 138.

⁵ J. Physiol., **38**, 343.

⁶ J. Chem. Soc., **95**, 1123.

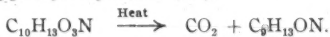
⁷ Oliver and Schäfer: J. Physiol., **18**, 230. Szymonowicz and Cybulski: Centralb. Physiol., **9**, 172.

⁸ Takamine: Am. J. Pharm., **73**, 535. Aldrich: Am. J. Physiol., **5**, 457. V. Furth: Sitzun. Wien., **1903**, 112; Monats. Chem., **34**, 261. Abel: Ber. d. chem. Ges., **36**, 1839; **37**, 368.

⁹ Pauly: Ber. d. chem. Ges., **36**, 2944; **37**, 1388; **41**, 4151; **42**, 484. Abderhalden and Bergell: *Ibid.*, **37**, 2022. Jowett: J. Chem. Soc., **85**, 192 (1904); **87**, 967 (1905). Bertrand: Compt. Rend., **139**, 502. Friedmann: Beitr. chem. Physiol. (Hofmeister), **6**, 92; **8**, 95. Stolz: Ber. d. chem. Ges., **37**, 4149; D. R. P.: 152,814 and 157,300. Mayer: Centralb., **1904**, II, 1744. Dakin: *Ibid.*, **1905**, II, 57. Böttcher: Ber. d. chem. Ges., **42**, 253.

¹⁰ Dzezgowski: Bull. Soc. Chim., [3] **12**, 911; Centralb., **1893**, II, 475.

Leger¹ separated from extracts of barley malt the alkaloid *hordenine*, $C_{10}H_{15}ON$, and its structure was established independently by him and by Gäbel,² who showed that it is *dimethyl-p-oxyphenylethylamine* (XII). A base found in nature, which apparently is closely related to hordenine, is *surinamine* (*ratanhine*, *angeline*, *geoffroyine* or *andirine*), which was first discovered by Hütter in the bark of *Geoffroya surinamensis*, Murr,³ and was employed as an anthelmintic. This same base has also been found in other plants by Wittstein,⁴ Ruge,⁵ Peckolt,⁶ Winckler,⁷ Gintyl⁸ and Kreitmair.⁹ The recent work of Blau¹⁰ seems to indicate that it is a higher homologue of tyrosine. He has shown that it decomposes, on heating above its melting point, giving a base which is isomeric with methyl-*p*-oxyphenylethylamine (XI):



XI.

Gautier¹¹ isolated a base having this same empirical constitution, $C_9H_{13}ON$, and also *p*-oxyphenylethylamine from sea water in which cod fish livers had been allowed to putrefy. So far as the writer is aware, no nitrogen methyl derivative of phenylethylamine has yet been found in plants or identified among the cleavage products of proteins.

Phenylethylamine¹² (VII) and *p*-oxyphenylethylamine¹³ (X)

¹ Compt. Rend., **142**, 108; **143**, 234, 916; **144**, 208, 488; Bull. Soc. Chim., [3] **35**, 235, 868, 1157; [4] **1**, 148; J. Pharm. Chim., [6] **23**, 177; **25**, 5, 273.

² Arch. Pharm., **244**, 435.

³ Magazin Pharm., **7**, 287.

⁴ Jahres. d. Chem., **1854**, 656.

⁵ Arch. Pharm., [2] **111**, 1; Z. Chem. Pharm., **1862**, 447; Centralb., **1868**, 1158; Jahres. d. Chem., **1862**, 493.

⁶ Z. oesterr. Apoth.-Ver., **1868**, 518.

⁷ Jahrb. d. Pharm., **2**, 159.

⁸ Sitzun. Wien., **58**, 443; Centralb., **1869**, 394.

⁹ Ann. Chem. (Liebig), **176**, 64.

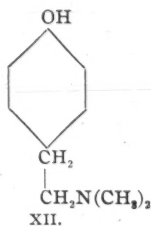
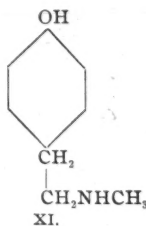
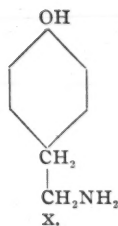
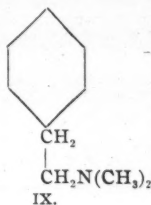
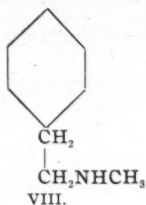
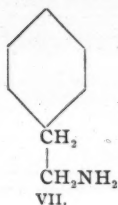
¹⁰ Z. physiol. Chem., **68**, 153.

¹¹ Bull. Soc. Chim., **35**, 1195 (1906); Centralb., **1907**, I, 546.

¹² Spica and Colombo: Gazz. Chim. Ital., **5**, 124. Berntsen: Ann. Chem. (Liebig), **184**, 304. Spica: Jahres. d. Chem., **1879**, 440. Ladenburg: Ber. d. chem. Ges., **19**, 783. Bischler and Napieralski: Ber. d. chem. Ges., **26**, 1905. Erlenmeyer and Lipp: Ann. Chem. (Liebig), **219**, 202. Schulze and Barbieri: J. prakt. Chem., [2] **27**, 346; Ber. d. chem. Ges., **14**, 1788; **16**, 1713. Hoffmann: Ber. d. chem. Ges., **18**, 2740. Hoogewerff and Dorp: Rec. Trav. Chim., **5**, 254. Henze: Ber. d. chem. Ges., **31**, 3065.

¹³ Schmitt and Nasse: Ann. Chem. (Liebig), **133**, 214.

are the only ones of the six amines represented below (formulas VII to XII), which have been synthesized.¹



We describe, in this paper, the preparation and properties of the second member of this series, *viz.*, *methylphenylethylamine* (VIII).

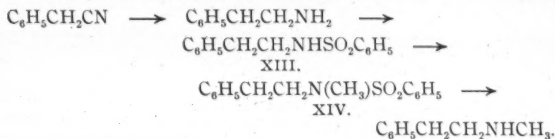
Phenylethylamine was prepared from benzyl cyanide by reduction with sodium and alcohol,² and converted into its benzenesulphone derivative (XIII) by treatment with benzenesulphone chloride in presence of alkali. The nitro-gen methyl derivative, *benzenesulphonemethylphenylethylamine* (XIV), was then prepared according to the directions of Hinsberg³ by the action of methyl iodide on the sodium salt of the amide.

¹ Since the completion of the experimental part of this paper, Barger (*loc. cit.*) has published a paper describing the preparation of *p*-oxyphenylethylamine by the reduction of *p*-oxybenzyl cyanide, $\text{HOC}_6\text{H}_4\text{CH}_2\text{CN}$. Pschorr, Wolfes and Buckow: *Ber. d. chem. Ges.*, **33**, 171.

² Ladenburg: *Loc. cit.*

³ *Ann. Chem. (Liebig)*, **265**, 183.

A quantitative yield of methylphenylethylamine was obtained by hydrolysis of this amide with hydrochloric acid at 150°–160°. The various transformations in this synthesis are represented by the following formulas:



Methylphenylethylamine (VIII) is a strong base which has a characteristic amine odor and absorbs carbon dioxide from the air. It boils at practically the same temperature, under diminished pressure, as phenylethylamine (VII) and is volatile with water, alcohol, and ether vapors. It is precipitated from an aqueous solution of its hydrochloride by the alkaloid reagents phosphotungstic acid and mercuric chloride, and gives a heavy brick-red precipitate with potassium-bismuth iodide. The picrate, picrolonate and platinum chloride salts are

Table I.

$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NH}_2$ (phenylethyl- amine). Melting points.	Derivatives.	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NHCH}_3$ (methylphenyl- ethylamine). Melting points.
217° ^{01,4}	Hydrochloride	152°–154°
255°–260°, with effer.	Platinum chloride salt	212°, with effervesc.
168° ⁰³	Picrate	141°
	Picrolonate	217°–218°
112° ⁰²	Urea = NCONH_2	141°
114° ⁰³	Phenylurea = $\text{NCONHC}_6\text{H}_5$	104°–105°
209°–210°	α -Naphthylurea = $\text{NCONHC}_{10}\text{H}_7$	106°
106° ⁰²	Phenylthiourea = $\text{NCSNHC}_6\text{H}_5$	113°–114°
68°–69°	Benzenesulphone = $\text{NSO}_2\text{C}_6\text{H}_5$	oil
65°–66°	<i>p</i> -Toluenesulphone = $\text{NSO}_2\text{C}_6\text{H}_4\text{CH}_3$	
181°	Acid oxalate	183°–184°

¹ Fileti and Piccini: Ber. d. chem. Ges., **12**, 1700. Haushofer: Jahres. d. Chem., **1883**, 703.

² Spica: Gazz. Chim. Ital., **9**, 568.

³ Bischler and Napieralski: Ber. d. chem. Ges., **26**, 1907. Michaelis and Linow: *Ibid.*, **26**, 2167.

⁴ Bertram and Walbaum: J. prakt. Chem., [2] **50**, 559.

difficultly soluble in water and have definite and sharp melting points. The melting points of a series of derivatives which are suitable for the identification of phenylethylamine and methylphenylethylamine are given in Table I. The physiological action of methylphenylethylamine is being investigated.

EXPERIMENTAL PART.

Phenylethylamine, $C_6H_5CH_2CH_2NH_2$.—We prepared this base according to Ladenburg's directions¹ by reduction of benzyl cyanide with sodium and ethyl alcohol. Of the various methods of preparation described in the literature, this appears to be the simplest and most practical.

Benzyl cyanide was dissolved in Kahlbaum's absolute alcohol (100 grams of the cyanide in 1200 cc. of alcohol) and the sodium (6 molecular proportions) slowly added to the hot alcohol solution. The mixture was then heated on the steam bath until all the sodium dissolved, cooled, and mixed with about one-fourth to one-third its volume of cold water. The excess of alcohol was then removed by distillation and the phenylethylamine separated from the alkaline fluid by steam distillation and converted into its hydrochloride. The crude salt which was obtained after evaporation was then decomposed with strong potassium hydroxide solution and the base extracted with ether, dried over stick potash, and purified by distillation under diminished pressure. Part of the benzyl cyanide underwent reduction by the sodium to toluene, with formation of ammonia and methylamine. Therefore, only about 65 per cent. of the crude salt obtained was pure phenylethylamine hydrochloride and the yield of amine was about 30-40 per cent. of the calculated. This yield was not increased by using more than 6 molecular proportions of sodium for the reduction. The yields obtained in six different preparations are given in Table II. The low yields in Experiments 1, 5 and 6 are explained by the fact that we used crude benzyl cyanide which was contaminated with a large amount of phenylacetamide.

¹ *Loc. cit.*

Table II.

	$C_6H_5CH_2CN$.	Alcohol.	Sodium.	Yield of crude hydrochloride.	Percentage of $C_6H_5CH_2CH_2NH_2$ HCl.	Yield of amine.	Per cent. of calculated.
	Grams.	cc.	Grams.	Grams.	Per cent.	Grams.	Per cent.
1	25.0	400.0	35.0	17.0	60.0	8.0	31.0
2	50.0	750.0	70.0	40.0	64.0	20.0	38.8
3	100.0	1200.0	120.0	70.0	82.2	45.0	43.7
4	100.0	1400.0	140.0	77.0	65.0	39.0	38.0
5	100.0	1200.0	120.0	65.0	62.0	31.5	30.5
6	100.0	1400.0	140.0			32.0	31.0

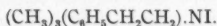
Action of Methyl Iodide on Phenylethylamine.—Methyl iodide reacts violently with this base. Two grams of the amine were dissolved in 25 cc. of ether and 2.2 grams (1 mol. = 2.26 grams) of methyl iodide, diluted with ether, added slowly to the solution of the base. There was an immediate reaction and in a few minutes the ether became turbid and an oil separated in drops which adhered to the sides of the flask. This finally solidified, on standing, in the form of plates. The mixture was heated to boiling for a few minutes to complete the reaction and the salt filtered off. It was extremely soluble in cold water and absolute alcohol but was precipitated from alcohol solutions by addition of ether. It crystallized in plates and was dried, for analysis, in a desiccator over potassium hydroxide and sulphuric acid. When heated in a capillary tube the salt begins to turn brown above 190° and decomposes at 235° – 236° . An iodine determination agreed with the calculated value for the *hydriodide of phenylethylamine*, $C_6H_5CH_2CH_2NH_2 \cdot HI$.

0.2122 gram of salt gave 0.1968 gram of AgI.

	$C_6H_{13}NI$.	Calculated for $C_6H_{14}NI$.	Found.
I	51.00	48.2	50.4

The ether filtrate, above, was allowed to concentrate by slow evaporation and a crystalline salt separated. This was less soluble in alcohol than the hydriodide described above and crystallized from hot alcohol in colorless plates

which melted at 227° to a clear oil without effervescence. A mixture of this salt and phenylethylamine hydriodide melted at 170° – 190° . The properties of this compound and an iodine determination indicated that it was a quaternary salt, or *trimethylphenylethylammonium iodide*,



0.1481 gram of salt gave 0.1194 gram of AgI.

	Calculated for $\text{C}_{11}\text{H}_{18}\text{NI}.$	Found.
I	43.64	43.56

1-Phenylethyl-2- α -naphthylurea,
 $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NHCONHC}_{10}\text{H}_7(\alpha)$.—Prepared by the action of α -naphthyl isocyanate on phenylethylamine. It is insoluble in water and crystallizes from hot 95 per cent. alcohol in needles felted together. It melts at 209° – 210° to an oil without effervescence. Analysis (Kjeldahl):

	Calculated for $\text{C}_{19}\text{H}_{23}\text{ON}_2.$	Found.
N	9.65	9.9

Benzenesulphonephenylethylamine,
 $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NHSO}_2\text{C}_6\text{H}_5$.—Practically a quantitative yield of this amide was obtained by dissolving molecular proportions of benzenesulphonechloride (51.2 grams) and phenylethylamine (35 grams) in benzene and then shaking this solution with an aqueous solution of potassium hydroxide (1.5 mols.). After the reaction was complete the benzene layer was removed and the excess of benzene expelled by heating on the steam bath. We obtained the amide as an oil which soon solidified on cooling. It is very soluble in alcohol, benzene, chloroform, and acetone, and insoluble in water. It was purified by crystallization from a mixture of benzene and petroleum ether. It separates from a hot, saturated alcohol solution in six-sided, tabular crystals melting at 68° – 69° to a clear oil. Analysis (Kjeldahl):

	Calculated for $\text{C}_{14}\text{H}_{15}\text{O}_2\text{NS}.$	Found.
N	5.36	5.21

p-Toluenesulphonephenylethylamine,
 $C_6H_5CH_2CH_2NHSO_2C_6H_4CH_3$.—This amide was prepared from *p*-toluenesulphonechloride and phenylethylamine in the same manner as the benzenesulphonephenylethylamine. It is very soluble in alcohol, acetone, chloroform, and benzene. It crystallizes from a mixture of benzene and petroleum ether in radiating needles, which melt at 65° – 66° to a clear oil. A mixture of the amide and the acid chloride (m. 69°) melted at 44° . Analysis (Kjeldahl):

	Calculated for $C_{18}H_{17}O_2NS$	Found.
N	5.09	5.00

Benzenesulphonemethylphenylethylamine,
 $C_6H_5CH_2CH_2(CH_3)N.SO_2C_6H_5$.—Sixty-five grams of benzenesulphonephenylethylamine were dissolved in 100 cc. of 95 per cent alcohol, and 11 grams of sodium hydroxide, dissolved in 15 cc. of water, added quickly to the alcohol solution. There was an immediate reaction and the sodium salt of the amide finally separated in colorless crystals. Forty-five grams of methyl iodide (1 mol. = 35.3 grams) were then added in small portions and the reaction allowed to take place at ordinary temperature. The salt reacted at once with the iodide, with evolution of heat, and it was necessary to heat only a few minutes, after the final addition of methyl iodide, in order to complete the reaction. The crude amide separated, on cooling, in the bottom of the flask as an insoluble oil which was dissolved in ether. More of the amide was obtained when the alcohol was diluted with water. After drying with calcium chloride and evaporating off the excess of ether the amide was obtained as a heavy oil, which did not crystallize after standing several days. We made no attempt to distil it under diminished pressure and the crude material was used in the following experiment. The yield of amide was practically quantitative.

Methylphenylethylamine, $C_6H_5CH_2CH_2NHCH_3$.—The crude amide from the preceding experiment was heated, under pressure, with 120 cc. of concentrated hydrochloric acid, at 150° – 160° for 2 hours. We obtained a clear solution which

was heated for several hours on the steam bath to remove the excess of hydrochloric acid, and then treated with an excess of strong aqueous potassium hydroxide solution. The base was extracted with ether, dried over potash, and then purified by distillation under diminished pressure. It boils at 112° – 115° at 36–40 mm. pressure. Analysis (Kjeldahl):

N	Calculated for		Found.	
	$C_9H_{13}N$.	$C_9H_{11}N$.	I.	II.
	10.37	11.57	10.24	10.30

The yield of pure distilled base was 27.0 grams. This did not, however, represent the total yield of base. We observed that this amine distills with ether vapors, and when hydrochloric acid gas was passed into the ether distillates the anhydrous hydrochloride of methylphenylethylamine separated in colorless plates melting at 152° – 154° to a viscous oil. When picric acid was added to an aqueous solution of this salt the characteristic picrate of methylphenylethylamine (see below) melting at 141° to an oil separated. About 2.5 grams of the base were recovered from the ether distillates.

Methylphenylethylamine is a strong base which absorbs carbon dioxide from the atmosphere. It has a distinct amine odor and shows a strong alkaline reaction with turmeric and litmus. It appears to be more soluble in water than phenylethylamine. It is precipitated from an aqueous solution by phosphotungstic acid and reacts with potassium-bismuth iodide, giving a brick-red precipitate. Addition of mercuric chloride to an aqueous solution of its hydrochloride gave a well crystallized mercury chloride double compound, which melted at 172° – 173° to an oil with no effervescence. This melting point was not raised by crystallization from water. The salt is not decomposed at its melting point and on cooling, it solidifies and then melts again at the same temperature. The gold chloride double salt is an oil.

Hydrochloride, $C_9H_9CH_2CH_2NHCH_3 \cdot HCl \cdot 2H_2O$.—This salt is extremely soluble in water and alcohol. It is very hygroscopic and the analytical determinations indicated that it contains two molecules of water of crystallization. It is

precipitated from alcohol, by addition of ether, in the form of plates which melt at 152° – 154° to a viscous oil with no effervescence. It was dried for analysis (Kjeldahl) in a desiccator over sulphuric acid:

	Calculated for $C_9H_{13}N.HCl.2H_2O$.	Found.
N	8.1	8.2

Picrate, $C_6H_5CH_2CH_2NHCH_3.C_6H_3O_7N_3$.—This salt was obtained when picric acid was added to an aqueous solution of the hydrochloride. It separated as an oil, which soon crystallized in prismatic crystals. They were badly etched, and melted at 141° to a clear oil with no effervescence. The salt does not contain water of crystallization. Analysis (Kjeldahl):

	Calculated for $C_9H_{13}N.C_6H_3O_7N_3$.	Found.
N	15.38	15.43

Picrolonate.—This salt is less soluble in water than the picrate. It crystallizes from water in two distinct forms according to the rate of cooling. When cooled quickly the salt separates in bunches of slender prisms or needles radiating from a common center. On the other hand, if the solution is allowed to cool slowly the salt deposits in large, tabular crystals. Both forms melt at 217° – 218° to a red oil with only slight effervescence.

Platinum Chloride Salt, $(C_6H_5CH_2CH_2NHCH_3.HCl)_2PtCl_4$.—Separates at once when hydrochloroplatinic acid is added to an aqueous solution of the hydrochloride. It crystallizes from hot water in characteristic, sharp-edged prisms, which melt at 212° with effervescence. It did not lose weight when heated at 100° – 110° for one hour. Analysis:

0.1456 gram of salt gave 0.0413 gram of Pt.

	Calculated for $(C_9H_{13}N.HCl)_2PtCl_4$.	Found.
Pt	28.67	28.35

Acid Oxalate, $C_6H_5CH_2CH_2NHCH_3.(COOH)_2$.—This salt was prepared by adding the base to a cold, saturated, aqueous solution of oxalic acid. It separated at once in glistening

plates, which melted at 183° – 184° to an oil with effervescence. It was dried at 60° – 70° for analysis (Kjeldahl):

	Calculated for $C_{20}H_{28}O_4N_2$.	$C_{11}H_{15}O_4N$.	Found.
N	7.77	6.22	6.33

1,1-Methylphenylethylurea, $C_6H_5CH_2CH_2(CH_3)N.CONH_2$.—

This was prepared by dissolving an excess of potassium cyanate in an aqueous solution of methylphenylethylamine hydrochloride and then evaporating the solution on the steam bath. The urea separated in colorless crystals and crystallized from hot water in plates melting at 141° to a clear oil with no effervescence. It is very soluble in boiling alcohol. Analysis (Kjeldahl):

	Calculated for $C_{10}H_{14}ON_2$.	Found.
N	15.73	15.55

1,1-Methylphenylethyl-2-phenylurea,

$C_6H_5CH_2CH_2(CH_3)NCONHC_6H_5$.—This was prepared by the action of phenyl isocyanate on methylphenylethylamine. It is insoluble in water and very soluble in hot alcohol and benzene. It crystallizes from 95 per cent. alcohol in rectangular plates which melt at 104° – 105° to a clear oil with no effervescence. Analysis (Kjeldahl):

	Calculated for $C_{16}H_{18}ON_2$.	Found.
N	11.02	10.75

1,1-Methylphenylethyl-2- α -naphthylurea,

$C_6H_5CH_2CH_2(CH_3)NCONHC_{10}H_7(\alpha)$.—From methylphenylethylamine and α -naphthyl isocyanate. It is very soluble in benzene and alcohol and difficultly soluble in water. It separates from hot 95 per cent. alcohol as an oil, which slowly crystallizes in rosettes of microscopic needles melting at 105° – 106° . It is precipitated from benzene by addition of petroleum ether. Analysis (Kjeldahl):

	Calculated for $C_{20}H_{20}ON_2$.	Found.
N	9.21	9.00

1,1-Methylphenylethyl-2-phenylthiourea,

$C_6H_5CH_2CH_2(CH_3)NCSNHC_6H_5$.—Phenyl isothiocyanate reacts

with methylphenylethylamine, giving a quantitative yield of this thiourea. It is difficultly soluble in water and crystallizes from 95 per cent. alcohol in bundles of long prisms, which melt at 113° – 114° to an oil. Analysis (Kjeldahl):

N	Calculated for	Found.
	$C_{16}H_{18}N_2S$.	
	10.37	10.17

NEW HAVEN, CONN.,
July, 1909.

[Contributions from the Sheffield Laboratory of Yale University.]

CLXXI.—RESEARCHES ON PYRIMIDINES:

DIMETHYL DERIVATIVES OF 2-AMINOPYRIMIDINE. PREPARATION OF 2-METHYLAMINO-5-METHYL- PYRIMIDINE.

[FORTY-SIXTH PAPER.]

BY TREAT B. JOHNSON AND KENNETH G. MACKENZIE.¹

This paper is a preliminary contribution to the study of aminomethylpyrimidines having the empirical formula $C_6H_9N_3$. Our interest in aminopyrimidines of this composition was incited by a paper entitled "Ueber die chemische Zusammensetzung der japanischen Soja-Souce oder Schōyu,"² in which the authors have described two decomposition products of *Schōyu* to which they have assigned the empirical formulas $C_6H_9N_3$ and $C_4H_{12}N_2$. They state that the substance, $C_6H_9N_3$, is probably an isomer of aminodimethylpyrimidine, but is not identical with any one of three pyrimidines of this constitution which have been described in the literature,³ viz., 2,6-dimethyl-4-aminopyrimidine,⁴ 2-amino-4,5-dimethylpyrimidine,⁵ and 2-amino-4,6-dimethylpyrimidine.⁶

¹ A part of this paper was presented as a thesis by Mr. Kenneth Gerard Mackenzie to the Faculty of the Graduate School of Yale University for the Degree of Master of Science (June, 1909).

² Suzuki, Aso, and Mitarai: Bull. Coll. Agriculture (Tokio Univ.), **7**, 477 (1907).

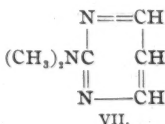
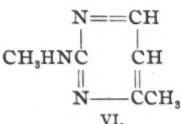
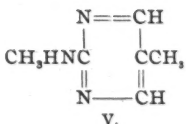
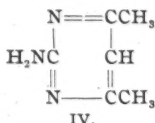
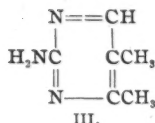
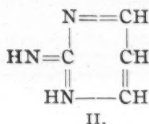
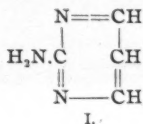
³ The Japanese investigators failed to recognize that a fourth isomer, 4,5-dimethyl-6-aminopyrimidine, has been prepared by Schlenker (Ber. d. chem. Ges., **34**, 2823). No salts of this pyrimidine have been described.—T. B. J.

⁴ Schwarze: J. prakt. Chem., **42**, 1 (1889). Schmidt: Ber. d. chem. Ges., **35**, 1577 (1902).

⁵ Schlenker: Ber. d. chem. Ges., **34**, 2819 (1901).

⁶ Angerstein: Ber. d. chem. Ges., **34**, 3962.

If we disregard the tautomeric form of 2-aminopyrimidine¹ (II), there are only five possible dimethyl derivatives of this pyrimidine (I), *viz.*, the two isomers described in the literature, 4,5-dimethyl² and 4,6-dimethyl-2-aminopyrimidine³ (III and IV), 2-methylamino-5-methylpyrimidine (V), 2-methylamino-4-methylpyrimidine (VI), and 2-dimethylaminopyrimidine (VII).



We shall describe, in this paper, the preparation and properties of 2-methylamino-5-methylpyrimidine (V), and also some derivatives of the isomeric 2-methylamino-4-methylpyrimidine (VI). A description of a new method of preparing thymine has also been appended to this paper.

It has been shown in several papers from this laboratory⁴ that aryl substituted aminopyrimidines can be obtained, in practically quantitative yields, by heating 2-mercaptopyrimidines with aromatic bases. The action of aliphatic amines on mercaptopyrimidines has not been investigated. Since

¹ Büttner: Ber. d. chem. Ges., **36**, 2229.

² Schlenker: *Loc. cit.*

³ Angerstein: *Loc. cit.*

⁴ Wheeler and Bristol: THIS JOURNAL, **33**, 438, 448. Johnson and Johns: *Ibid.*, **34**, 175. Johnson and Heyl: *Ibid.*, **38**, 238. Johnson and Storey: *Ibid.*, **40**, 131.

it was necessary for us to devise a practical method of preparing alphyaminopyrimidines easily and in sufficient quantities for our work, we therefore investigated the action of methylamine on some 2-mercaptopyrimidines.

We now find that 2-methylmercapto-5-methyl-6-oxypyrimidine¹ (VIII), and 2-methylmercapto-4-methyl-6-oxypyrimidine² (IX), react with methylamine at 140°–150°, giving quantitative yields of 2-methylamino-5-methyl-6-oxypyrimidine (X) and 2-methylamino-4-methyl-6-oxypyrimidine (XI), respectively. The latter pyrimidine was identical with the 2-methylaminopyrimidine obtained by Jäger³ by alkylation of 2-amino-4-methyl-6-oxypyrimidine⁴ with methyl iodide. The same pyrimidine has also recently been prepared by Majima⁵ by condensing methylguanidine with ethyl acetoacetate. The yield by this method, however, corresponds to only about 50 per cent. of the theoretical, because part of the methylguanidine condenses, giving the isomeric 2-amino-3,4-dimethyl-6-oxypyrimidine.

These two 2-methylaminopyrimidines, (X) and (XI), reacted smoothly with phosphorus oxychloride, giving practically quantitative yields of 2-methylamino-5-methyl-6-chloropyrimidine (XII) and 2-methylamino-4-methyl-6-chloropyrimidine (XIII), respectively. Both of these pyrimidines underwent hydrolysis to the original 6-oxypyrimidines (X) and (XI), when an attempt was made to reduce them with hydriodic acid. On the other hand, they were converted into 2-methylamino-5-methylpyrimidine (V) and 2-methylamino-4-methylpyrimidine (VI), respectively, by reduction with zinc dust. We have not isolated the free 2-methylamino-4-methylpyrimidine,⁶ but have procured evidence of its formation, since we have obtained a picrate of the base and a characteristic zinc chloride double compound of definite

¹ Wheeler and Merriam: *THIS JOURNAL*, **29**, 487.

² List: *Ann. Chem. (Liebig)*, **236**, 12.

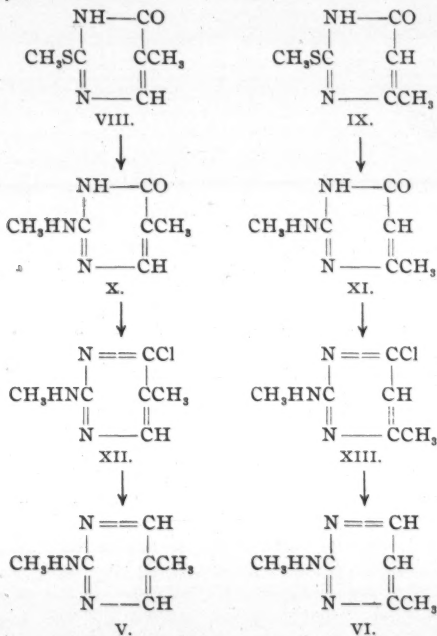
³ *Ann. Chem. (Liebig)*, **262**, 365.

⁴ Jäger: *Loc. cit.* Köhler: *Ber. d. chem. Ges.*, **19**, 220.

⁵ *Ber. d. chem. Ges.*, **41**, 176.

⁶ We were obliged to discontinue experiments on the reduction of 2-methylamino-4-methyl-6-chloropyrimidine, because of the unexpected departure of one of us from the laboratory and on account of pressure of other work.—T. B. J.

constitution. The experimental evidence indicates that this methylaminopyrimidine is not identical with the base found in *Schöyu*.



2-Methylamino-5-methylpyrimidine (V) is not identical with the base $\text{C}_6\text{H}_8\text{N}_2$, which Suzuki and his coworkers isolated from *Schöyu*. They state that their base reacted with diazobenzenesulphonic acid, in the presence of alkali, giving an intense red color. Our pyrimidine and the diazo reagent gave at first no color, but on long standing a brilliant red color finally developed. A characteristic feature of their base was its tendency to form acid salts, viz., the picrate

$C_6H_9N_3(C_6H_3O_7N_3)_2$, decomposing at 230° , and the hydrochloride $C_6H_9N_3 \cdot 2HCl$, melting at 232° – 233° . Our pyrimidines, on the other hand, are characterized by their tendency to form basic salts. The isomeric picrates, $(C_6H_9N_3)_2 \cdot C_6H_3O_7N_3$, of 2-methylamino-5-methylpyrimidine and 2-methylamino-4-methylpyrimidine both decomposed when heated above 150° . 2-Methylamino-5-methylpyrimidine formed a hydrous hydrochloride, $(C_6H_9N_3)_2 \cdot HCl \cdot H_2O$, melting at 162° – 163° . It is an interesting fact that 2-amino-5,6-dimethylpyrimidine¹ is the only dimethyl derivative of 2-aminopyrimidine, so far examined, that forms acid salts, viz., the picrate and hydrochloride.

A New Method of Preparing Thymine.

In a previous paper from this laboratory one of the writers² showed that pseudomethylthiourea condenses smoothly, in aqueous solution, with the sodium salt of diethyl oxalpropionate, giving 2-methylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine. When this acid, in small quantities, is heated above its melting point it undergoes a quantitative decomposition, with evolution of carbon dioxide, giving 2-methylmercapto-5-methyl-6-oxypyrimidine.³ A quantitative yield of thymine is then obtained by hydrolysis of this mercapto-pyrimidine. The writer did not, at that time, lay stress on this method of synthesizing thymine because of the progress of other work in this laboratory on different methods of preparing this pyrimidine.

We have now investigated this method of preparation and find that the sodium salt of diethyl oxalpropionate condenses as smoothly, in aqueous solution, with pseudoethylthiourea as with pseudomethylthiourea, giving the corresponding 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine (XIV). This pyrimidine melts lower than the corresponding 2-methylmercapto compound⁴ and undergoes decomposition at its melting point, giving 2-ethylmercapto-5-methyl-6-oxypyrimi-

¹ *Loc. cit.*

² Johnson: *J. Biol. Chem.*, **3**, 299 (1907).

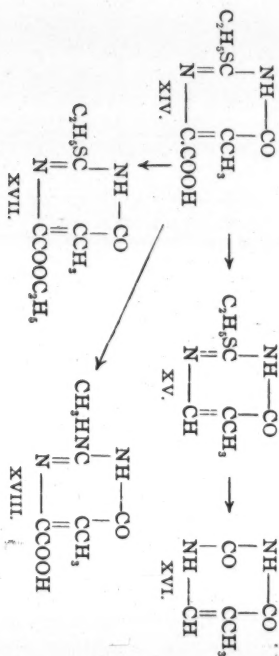
³ Wheeler and Merriam: *Loc. cit.*

⁴ Johnson: *Loc. cit.*

dine¹ (XV), which can be converted into thymine (XVI) by hydrolysis with hydrochloric acid. The success of this method of preparation was evidently dependent upon the fact whether large amounts of the mercapto acid (XIV) could be changed smoothly and quantitatively into 2-ethylmercapto-5-methyl-6-oxypyrimidine.² Working with small quantities, less than 15-16 grams of the acid, the decomposition into 2-ethylmercapto-5-methyl-6-oxypyrimidine was practically quantitative and the final yield of thymine corresponded to nearly 85-90 per cent. of the theoretical. On the other hand, when large amounts of 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine are decomposed under the same conditions the method is not practicable because it is then necessary to heat a long time, at a high temperature, in order to complete the reaction. Under such conditions secondary reactions set in with formation of products which contaminate the 2-ethylmercapto-5-methyl-6-oxypyrimidine and render its purification difficult. It is probable that these mercaptoprimidines, when heated at high temperatures and in presence of impurities, slowly undergo dissociation into ethylene hydrocarbons and 2-thiopyrimidines. The ethyl ester of 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine (XVII) was obtained in one experiment as the chief product of the condensation. It was also formed quantitatively by the action of ethyl iodide on the silver salt of the mercapto acid (XIV). When the mercapto acid (XIV) was heated with methylamine, a quantitative yield of 2-methylamino-4-carboxyl-5-methyl-6-oxypyrimidine (XVIII) was obtained. These various transformations are represented by the following formulas:

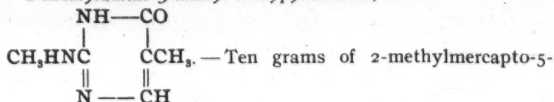
¹ Wheeler and Johnson: *THIS JOURNAL*, **31**, 595.

² *Loc. cit.*



EXPERIMENTAL PART.

2-Methylamino-5-methyl-6-oxypyrimidine,



methyl-6-oxypyrimidine¹ were heated with 18 grams of 33 per cent. methylamine solution (6 grams CH_3NH_2) at 140° – 150° for two hours. The clear solution was then transferred to a dis-

¹ Loc. cit.

tillation flask and the excess of methylamine expelled by passing a current of air through the boiling solution. On cooling, 8 grams of the aminopyrimidine separated, corresponding to 91 per cent. of the theoretical yield. In two other experiments, when 6 grams of the 2-methylmercaptopyrimidine were heated with 7.2 grams of 33 per cent. methylamine solution, under the same conditions, we obtained 5.0 and 5.3 grams of the crude pyrimidine.

This 2-methylaminopyrimidine is difficultly soluble in cold, but very soluble in hot water; soluble in boiling alcohol and benzene. It crystallizes from water in colorless, hairy crystals, which melt at 213° to a clear oil. The pyrimidine is characterized by its tendency to form supersaturated, aqueous solutions. It reacts with diazobenzenesulphonic acid in presence of sodium hydroxide, giving a strong, claret-red color. It contained one molecule of water of crystallization, which was determined by heating at 100° – 110° for one hour.

0.5821 gram substance lost 0.0584 gram H_2O .

	Calculated for $C_6H_9ON_3 \cdot H_2O$.	Found.
H_2O	11.4	10.03

Nitrogen determination in anhydrous substance (Kjeldahl):

	Calculated for $C_6H_8ON_3$.	Found.
N	30.22	30.23

Sulphate, $C_6H_8ON_3 \cdot H_2SO_4$.—Five-tenths gram of the pyrimidine base and 0.7 gram of sulphuric acid were dissolved in water and the solution allowed to concentrate in the air. The salt finally crystallized in large, transparent, tabular crystals, which melted at 202° to a brown oil. The salt is insoluble in alcohol but very soluble in water. It was dried at 100° for analysis (Kjeldahl):

	Calculated for $C_6H_8ON_3 \cdot H_2SO_4$.	I.	Found.	II.
N	17.72	17.51		17.83

Picrate, $(C_6H_8ON_3)_2 \cdot C_6H_3O_7N_3 \cdot H_2O$.—This salt was prepared by adding a solution of picric acid to an aqueous solution of the base. The picrate deposited in distorted prisms

which melted with decomposition at 240° . Analysis (Kjeldahl):

Calculated for $C_6H_9ON_3, C_6H_3O_7N_3$ = 22.82 per cent N.
 Calculated for $C_6H_9ON_3, (C_6H_3O_7N_3)_2$ = 21.10 per cent N.
 Calculated for $(C_6H_9ON_3)_2, C_6H_3O_7N_3, H_2O$ = 24.00 per cent N.

	I.	II.	III.	IV.
Nitrogen found:	23.89	24.12	24.20	24.25

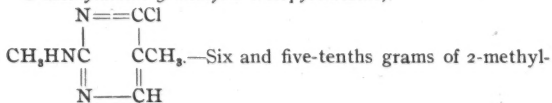
Platinum Chloride Salt, $(C_6H_9ON_3, HCl)_2, PtCl_4$, was prepared by addition of hydrochloroplatinic acid to an aqueous solution of the pyrimidine base. It did not contain water of crystallization. Platinum determinations:

I. 0.0889 gram of salt gave 0.0248 gram of Pt.

II. 0.0989 gram of salt gave 0.0277 gram of Pt.

	Calculated for $(C_6H_9ON_3, HCl)_2, PtCl_4$.	I.	Found.	II.
Pt	28.3	27.90		28.06

2-Methylamino-5-methyl-6-chlorpyrimidine,

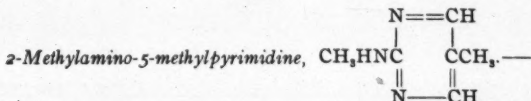


amino-5-methyl-6-oxypyrimidine were dissolved, by warming, in 30 cc. of phosphorus oxychloride and the solution boiled for 30 minutes. The excess of phosphorus oxychloride was then removed by heating at 100° under diminished pressure, when a viscous liquid was obtained. This was dissolved in cold water and the solution made alkaline with sodium hydroxide, when the chlorpyrimidine separated. After drying in a vacuum over concentrated sulphuric acid it weighed 6.9 grams, corresponding to 95 per cent. of the theoretical. In a second experiment, when we used 10.6 grams of the 2-methylmercaptopyrimidine and 53 cc. of phosphorus oxychloride we obtained a yield of 11.5 grams of the chlorpyrimidine.

The pyrimidine is insoluble in water but soluble in alcohol and benzene. It sublimes at 100° and melts at 131° to a

clear oil with no effervescence. It crystallizes from 95 per cent. alcohol in prismatic crystals. Analysis (Kjeldahl):

	Calculated for $C_5H_8N_2Cl$	Found.
N	26.67	26.83



Five grams of 2-methylamino-5-methyl-6-chloropyrimidine and 15 grams of zinc dust were suspended in 200 cc. of water and the mixture digested for 8 hours. The excess of zinc was then removed by filtration and the filtrate concentrated on the steam bath. We obtained a thick syrup which was dissolved in 25 cc. of water and an excess of a saturated, aqueous solution of potassium hydroxide added. A light colored precipitate was formed which was filtered by suction, and dried in a desiccator over sulphuric acid.

An attempt to purify this substance by sublimation was unsuccessful. The crude, dry material was finally extracted several times with boiling ether. When the excess of ether was evaporated, about 2 grams of a colorless, crystalline substance which melted at 97° – 100° to a clear oil was obtained. In order to purify it for analysis it was dissolved in dry ligroin and the solution allowed to concentrate by slow evaporation. The pyrimidine separated under these conditions in beautiful, transparent prisms, which melted sharply at 102° to a clear oil. The pyrimidine is extremely soluble in cold water, ether, and benzene. It showed no alkaline reaction when tested with turmeric and was precipitated from an aqueous solution by mercuric chloride. It gave at first no color when tested with diazobenzenesulphonic acid, but on allowing the mixture to stand a strong red color finally developed. The pyrimidine sublimates when heated above 100° . Analysis:

	Calculated for $C_6H_8N_2$	Found.
N	34.14	34.20

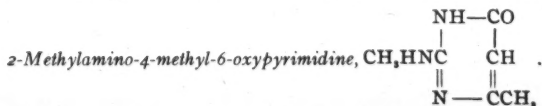
An attempt was made to reduce the 6-chlorpyrimidine with hydriodic acid, but it underwent hydrolysis, giving 2-methylamino-5-methyl-6-oxypyrimidine.

Picrate, $(C_6H_5N_3)_2 \cdot C_6H_5O_7N_3$.—This salt separated immediately when an aqueous solution of picric acid was added to a solution of the pyrimidine base. It had no definite melting point, but began to shrivel at about 100° and decomposed when heated above 150° . Analysis:

	Calculated for $(C_6H_5N_3)_2 \cdot C_6H_5O_7N_3$	Found.
N	26.53	26.36

Hydrochloride, $(C_6H_5N_3)_2 \cdot HCl \cdot H_2O$.—This salt was prepared by dissolving the base in warm hydrochloric acid and concentrating the solution on the steam bath. It was extremely soluble in water, but crystallized from methyl alcohol in well-developed prismatic crystals. The salt melts at 162° – 163° to a clear oil and does not effervesce below 250° . Analysis:

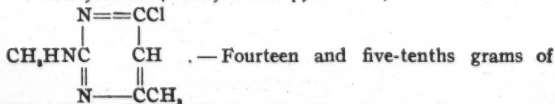
	Calculated for			Found.	
	$C_6H_5N_3 \cdot HCl$	$C_6H_5N_3 \cdot 2HCl$	$(C_6H_5N_3)_2 \cdot HCl \cdot H_2O$	I.	II.
N	26.33	21.64	27.95	27.7	27.88



—We prepared this pyrimidine¹ by heating 2-methylmercapto-4-methyl-6-oxypyrimidine¹ with an excess of methylamine at 140° – 150° . The yield was quantitative and the pyrimidine melted at 201° – 202° after one recrystallization from hot water. Analysis (Kjeldahl):

	Calculated for $C_4H_8ON_2$	Found.
N	30.22	30.00

2-Methylamino-4-methyl-6-chlorpyrimidine,



¹ Loc. cit.

2-methylamino-4-methyl-6-oxypyrimidine and 72 cc. of phosphorus oxychloride were heated in an oil bath at 120°-130° for 30 minutes, when the evolution of hydrochloric acid gas had practically ceased. We obtained a clear solution which was then heated at 100° under diminished pressure to remove the excess of phosphorus oxychloride. A brown oil remained, which was dissolved in cold water, and the solution made alkaline with sodium hydroxide. The pyrimidine separated in colorless crystals and was dried in a desiccator over sulphuric acid. It is very insoluble in water but easily soluble in alcohol. It separates from an alcohol solution in long needles which melt at 135° to a yellow oil without effervescence. It slowly sublimes when heated above 100°. Analysis (Kjeldahl):

	Calculated for $C_8H_8N_2Cl$	Found.
N	26.67	26.70

Reduction of 2-Methylamino-4-methyl-6-chlorpyrimidine with Zinc.—This chlorpyrimidine is very slowly reduced by digestion with zinc dust because of the insolubility of the pyrimidine in water. Unaltered chlorpyrimidine was recovered after 12 hours' digestion of 12 grams of the pyrimidine and 50 grams of zinc dust in 1000 cc. of water. One hundred cc. of alcohol were then added and the mixture boiled again for 10 hours, cooled and filtered. By extraction of the zinc residue with alcohol, we recovered 6 grams of unaltered 6-chlorpyrimidine. The aqueous filtrate was concentrated to a volume of 15-20 cc. and allowed to stand at ordinary temperature, when well-developed, red crystals separated. They melted sharply at 170°-172° to an oil without effervescence and contained zinc and chlorine. The substance was extremely soluble in water and did not lose weight when heated at 100°-110°. A nitrogen determination (Kjeldahl) agreed with the calculated value for a double compound containing 3 molecules of 2-methylamino-4-methylpyrimidine and one molecule of zinc chloride, $(C_8H_8N_2)_3 \cdot ZnCl_2$:

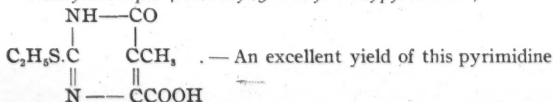
	Calculated for $(C_8H_8N_2)_3 \cdot ZnCl_2$	Found.
N	22.97	22.80

The filtrate obtained after separation of the zinc chloride compound was concentrated on the steam bath to a viscous liquid and then triturated with about 25 cc. of a strong, aqueous solution of potassium hydroxide. An amorphous substance was precipitated, which was separated by suction filtration, washed with a few drops of cold water, and dried in a desiccator over sulphuric acid. This substance was then extracted in a Soxhlet apparatus with ether for three days. When the ether was evaporated we obtained an oil which dissolved at once in water, alcohol and benzene. In order to establish the presence of 2-methylamino-4-methylpyrimidine, the oil was dissolved in water and a solution of picric acid added to the aqueous solution. A picrate separated at once in the form of irregular prisms which melted at 150° – 155° to an oil with no appreciable effervescence. This salt did not give a test for chlorine. Analysis (Kjeldahl):

	Calculated for (C ₆ H ₉ N ₃) ₂ .C ₆ H ₅ O ₇ N ₃ .		Found.
N	26.5	23.8	25.98

2-Methylamino-4-methyl-6-chlorpyrimidine was converted into 2-methylamino-4-methyl-6-oxypyrimidine when heated with hydriodic acid.

2-Ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine,



is obtained by condensation of pseudoethylthiourea with the sodium salt of diethyl methyloxalacetate in aqueous solution. In our preliminary experiments this sodium salt was prepared by condensation of diethyloxalate with ethyl propionate in presence of sodium ethylate.¹ We found, however, that the use of dry sodium ethylate is unnecessary and that as good a yield of the salt can be obtained by condensation of the esters in anhydrous ether in presence of metallic sodium. This fact is shown by comparison of the yields of pyrimidine given in the table. Our method of preparing the pyrimidine

¹ Arnold: Ann. Chem. (Liebig), **246**, 329.

was as follows: A mixture of 50 grams of ethyl propionate and 71 grams of diethyl oxalate was added slowly to dry ether, in which was suspended 11.5 grams of metallic sodium. After the esters had been added the mixture was allowed to stand about 2 days to insure a complete reaction. Cold water (about 500-600 cc.) was then cautiously added to dissolve the sodium salt, and the ether layer separated. To this aqueous solution was then added a concentrated, aqueous solution of 52 grams of pseudoethylthiourea hydrobromide and finally two molecular proportions of potassium hydroxide (32 grams). After allowing to stand for 2 days at 40°-50° the solution was concentrated to about one-half its original volume, cooled, and acidified with an excess of strong hydrochloric acid. The pyrimidine usually separated in the form of a light pink or nearly colorless, granular powder melting at 210°-215° with evolution of carbon dioxide. The yield of mercaptopyrimidine is decreased by using, for the condensation, more than two molecular proportions of potassium hydroxide because the pyrimidine is slowly converted into thymine-4-carboxylic acid,¹ with evolution of ethyl mercaptan, when warmed with strong alkaline solutions (Experiment 5 in table).

The proportion of pseudoethylthiourea hydrobromide to be used for a condensation was calculated upon the basis that the yield of sodium salt of diethyl oxalpropionate is only about 50 per cent. of the theoretical (Arnold² says 45 per cent.). Under these conditions, fifty grams of ethyl propionate require for condensation 45 grams of the pseudothiourea salt, which we increased to 52-54 grams or about 0.6 molecular proportion. The yield of pyrimidine was not increased by using more than this proportion (see Experiment 2 in table).

¹ Johnson: J. Biol. Chem., 8, 299.

² Loc. cit.

Table I.

	$\text{CH}_3\text{CH}_2\text{COOC}_2\text{H}_5$ Grams.	$(\text{COOC}_2\text{H}_5)_2$ Grams.	Na used. Grams.	$\text{C}_2\text{H}_5\text{SC}(\text{NH})\text{NH}_2$ HBr. Grams.	KOH used. Grams.	Yield of 2-mercapto-4-carboxyl-5-methyl-6-oxypyrimidine. Grams.
1	50.0	71.0	11.5	52.0	16.0	36.0
2	50.0	71.0	11.5	72.0	22.0	36.5
3	50.0	71.0	11.5	54.0	32.0	34.0
4	50.0	71.0	11.5 in form NaOC_2H_5	54.0	32.0	37.0
5	100.0	144.0	22.5	100.0	108.0 (2.5 mols.)	60.0 and 15.0 of thymine-4-carboxylic acid ¹
6	50.0	71.0	11.5 in form NaOC_2H_5	45.0	30.0	22.0

2-Ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine is soluble in boiling water but separates on cooling in clusters of slender needles and prismatic crystals. It is more soluble in alcohol than in water. It decomposes, after crystallization from water, from 215° – 218° with effervescence, giving 2-ethylmercapto-5-methyl-6-oxypyrimidine² (see below). If the acid is dissolved in dilute sodium hydroxide solution and reprecipitated by addition of hydrochloric acid it separates in colorless crystals melting sharply at 220° . The acid is not precipitated from aqueous solutions of its sodium salt by addition of acetic acid.

Analysis (Kjeldahl):

	Calculated for $\text{C}_8\text{H}_{10}\text{O}_2\text{N}_2\text{S}$.	I.	Found.	II.
N	13.08	13.3		13.2

Stability of the Sodium Salt of Diethyl Oxalpropionate, $\text{C}_2\text{H}_5\text{OOC.C}(\text{ONa}).\text{C}(\text{CH}_3)\text{COOC}_2\text{H}_5$.—Seventy-one grams of diethyl oxalate were condensed with 50 grams of ethyl propionate, in presence of sodium ethylate,³ on June 10, 1908. This salt was then allowed to stand exposed to the air, in an

¹ Johnson: *Loc. cit.*

² *Loc. cit.*

³ Arnold: *Loc. cit.*

open flask, until October 15, 1908. It was then condensed with pseudoethylthiourea in the usual manner, when we obtained 22 grams of pyrimidine melting at 209° – 214° (Experiment 6 in table).

Ethyl Ester of 2-Ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine,

$$\begin{array}{c} \text{NH}-\text{CO} \\ | \quad | \\ \text{C}_2\text{H}_5\text{SC} \quad \text{CCH}_3 \\ || \quad || \\ \text{N}-\text{CCOOC}_2\text{H}_5 \end{array}$$

—The sodium salt of diethyl

oxalpropionate was prepared in the usual manner by condensing 71 grams of diethyl oxalate with 50 grams of ethyl propionate in presence of metallic sodium. This salt was then dissolved in 400–500 cc. of water and mixed with an aqueous solution containing 0.6 molecular proportion of pseudoethylthiourea. The mixture was then allowed to stand, at ordinary temperature, for several days, when 17.0 grams of the ethyl ester had separated. After concentrating the aqueous filtrate and then acidifying with hydrochloric acid, we obtained the corresponding acid. This ester is difficultly soluble in water but very soluble in boiling alcohol. It crystallizes from 95 per cent. alcohol in prisms which melt at 172° – 173° to a clear oil. It dissolves in sodium hydroxide solution without decomposition but on warming it easily undergoes saponification. The ester is also formed quantitatively by the action of ethyl iodide on the silver salt of 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine. Analysis (Kjeldahl):

	Calculated for $\text{C}_{10}\text{H}_{14}\text{O}_2\text{N}_2\text{S}$	Found.
N	11.56	11.8

Behavior of 2-Ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine on Heating.—A few grams of this mercaptopyrimidine (3–4 grams) were heated in an oil bath at 220° – 230° until effervescence ceased. A dark oil was obtained which solidified on cooling. This substance was purified by crystallization from hot water and separated in prisms melting at 159° . It was identified as 2-ethylmercapto-5-methyl-6-oxypyrimidine.¹ Analysis (Kjeldahl):

¹ Wheeler and Johnson: *Loc. cit.*

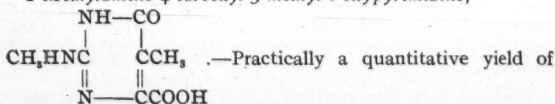
	Calculated for $C_7H_{10}ON_2S$.	Found.
N	16.47	16.6

Conversion of 2-Ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine into Thymine.—Sixteen grams of this mercapto-pyrimidine, melting at 218° – 220° , were heated in an oil bath at 220° – 230° until the evolution of carbon dioxide ceased (about 1.5 hours). We obtained 13.0 grams of crude 2-ethylmercapto-5-methyl-6-oxypyrimidine (theoretical yield is 12.7 grams), which was then digested for several hours with concentrated hydrochloric acid and converted into thymine. The acid solution was evaporated to dryness and the crude thymine decolorized in hot, aqueous solution with animal charcoal and then crystallized from water. It separated in colorless crystals, decomposing at about 325° – 335° . The yield was 8.0 grams, or about 85 per cent. of the theoretical. Since 36–37 grams of 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine can be obtained from 50 grams of ethyl propionate (see table) this amount of thymine (8 grams) therefore corresponds to 21.6 grams of the ester.

A quantitative yield of thymine from 21.6 grams of ethyl propionate would be 26.5 grams. Analysis (Kjeldahl):

	Calculated for $C_8H_{10}O_2N_2$.	Found.
N	22.22	22.00

2-Methylamino-4-carboxyl-5-methyl-6-oxypyrimidine,



this pyrimidine was obtained when 7 grams of 2-ethylmercapto-4-carboxyl-5-methyl-6-oxypyrimidine and 9 grams of a 33 per cent. solution of methylamine were heated at 140° – 150° for 4 hours. It was precipitated from cold, aqueous solutions of its sodium, ammonium and methylamine salts by addition of acetic acid. It was very insoluble in cold water and crystallized from hot water in long, hairy crystals which melted

at 270°–280°, according to the rate of heating, with effervescence. Analysis (Kjeldahl):

	Calculated for $C_7H_9O_3N_3$	Found.
N	22.9	22.4

Methylamine Salt, $C_7H_9O_3N_3 \cdot CH_3NH_2$.—This salt crystallized from hot water in granular crystals, which decomposed with violent effervescence at 274°. Two of the crystals that were used for analysis weighed 0.0393 and 0.03170 gram, respectively. Analysis (Kjeldahl):

	Calculated for $C_7H_9O_3N_3 \cdot CH_3NH_2$	Found.
N	26.1	25.91

Hydrochloride, $C_7H_9O_3N_3 \cdot HCl$.—This salt was prepared by dissolving the pyrimidine base in hot, dilute hydrochloric acid and allowing the solution to cool. The salt separated in prismatic crystals, which decomposed at 276°–283° with effervescence. Analysis (Kjeldahl):

	Calculated for $C_7H_9O_3N_3 \cdot HCl$	Found.
N	19.14	19.32

NEW HAVEN, CONN.,
June 1, 1909.

REVIEWS.

JAHREBUCH DER CHEMIE. BERICHT ÜBER DIE WICHTIGSTEN FORTSCHRITTE DER REINEN UND ANGEWANDTEN CHEMIE. Unter Mitwirkung von H. BECKURTS, Braunschweig, C. A. BISCHOFF, Riga, M. DELBRÜCK, Berlin, J. M. EDER, Wien, P. FRIEDLÄNDER, Wien, C. HÄUSSERMANN, Ludwigsburg, A. HERZFELD, Berlin, K. A. HOFMANN, München, G. KEPPELER, Hannover, J. LEWKOWITSCH, London, A. MORGEN, Hohenheim, B. NEUMANN, Darmstadt, M. NIERENSTEIN, Liverpool, O. SACKUR, Breslau, K. SPIRO, Strassburg i. E., herausgegeben von RICHARD MEYER, Braunschweig. XVII. Jahrgang, 1907. Braunschweig: Friedrich Vieweg und Sohn. 1908. Price, M. 16.

The editor of this excellent and helpful publication calls attention to the fact that the chapter on "Physical Chemistry" has been prepared by Dr. O. Sackur, that the report on "Metallurgy" has been written by Professor B. Neumann, of Darmstadt; and that the chapter on the "Inorganic Chemical Industries," hitherto prepared by Dr. F. Quincke, has now been written by Dr. G. Keppler. He further states that technical chemical processes in which the electric current is the source of energy are thoroughly dealt with in the sections on "Metallurgy" and "Inorganic Chemical Industries."

The eighteen chapters of the book have the titles given below: I., Physical Chemistry; II., Inorganic Chemistry; III., Organic Chemistry; IV., Physiological Chemistry; V., Pharmaceutical Chemistry; VI., Chemistry of Foods; VII., Agricultural Chemistry; VIII., Fuels and Explosives; IX., Metallurgy; X., Inorganic Chemical Industries; XI., Technology of the Carbohydrates; XII., Fermentation Industries; XIII., Technology of Fats and Petroleum; XIV., Coal Tar and Dyestuffs, I.; XV., Coal Tar and Dyestuffs, II.; XVI., Chemical Technology of the Spinning Industries; XVII., Tanning; XVIII., Photography.

So far as the writer of this notice has been able to examine the volume, it appears to be of the same high merit as the earlier volumes, and it will be welcomed by the many who have used them.

I. R.

KURZES LEHRBUCH DER ORGANISCHEN CHEMIE. VON PROF. DR. A. BERNTHSEN, Grossherzogl. Bad. Hofrat, Direktor der Badischen Anilin- und Soda-Fabrik, Ludwigshafen am Rhein, Früher Professor an der Universität zu Heidelberg. Zehnte Auflage. Bearbeitet in Gemeinschaft mit Dr. ERNST MOHR, A. O. Professor an der Universität Heidelberg. Braunschweig: Friedr. Vieweg und Sohn. pp. 640. Price, M. 12.

In his preface the author says: "Although the tenth edition differs in appearance but slightly from the preceding, nevertheless the numerous advances in organic chemistry have been thoroughly taken into account, while an increase in the length of the book has been avoided by means of abbreviations in other parts. Bernthsen's "Organic Chemistry" is so favorably known that it is not necessary to tell chemists about it. There is no better book for the student who has already had an introduction to the subject. A careful study of each chapter will give him a very fair idea of the extent to which the subject has been developed, of the methods that have been used, and of the speculations that have resulted from a study of the facts. The chief objection to the book is its compactness. It is very strong meat and must be partaken of in small quantity at a time or indigestion will result. Take, for example, the sections entitled *Konstitution des Benzols*; *Benzoltheorie* and *Spezielle Benzolformeln*. There is certainly not a superfluous word in these sections. The question is, Are there enough words to make the treatment clear? Probably not. But there are references to the most important articles and books bearing on the subject, and the earnest student who wants to know will be able to work out the problem by studying the book and the literature referred to. The same general remarks may be made in regard to all the other sections of the book, and it thus appears that Bernthsen's

"Organic Chemistry" serves a double purpose. It is a condensed text-book and a sensible, eclectic guide to the literature, and, as such, can be highly recommended to all students of chemistry.

I. R.

NEUERE THEORETISCHE ANSCHAUUNGEN AUF DEM GEBIETE DER ORGANISCHEN CHEMIE. Von Dr. FERDINAND HENRICH, A. O. Professor an der Universität Erlangen. Braunschweig: Friedr. Vieweg und Sohn. 1908. pp. 194. Price, M. 7.

This is a very interesting and valuable book that should be in the hands of every advanced student of chemistry. The subjects in the sixteen chapters are:

I. Lavoisier's dualistic views; II. The later theory of types and the first attack by Kekulé; III. van't Hoff's hypothesis regarding the form of the carbon atom; IV. Thiele's hypothesis of the partial valences; V. Attacks upon Thiele's theory; VI. Researches on the so-called negative nature of atomic groups; VII. Tautomerism and desmotropism; VIII. Pseudo acids, pseudo bases and ionization isomerism; IX. Color and chemical constitution; X. Fluorescence and chemical constitution; XI. Molecular rearrangements; XII. Basic properties of oxygen; XIII. J. U. Nef's theoretical views; XIV. A. Michael's theoretical system; XV. A. Werner's theory; XVI. Later electrochemical views.

Most of these chapters are summaries of the articles that have appeared in the journals. The summaries are clear and show that the author has read the articles with care. For the earnest student of chemistry, whether he is a university student in the narrower sense or a student in the broader and higher sense, the book will be of great value.

It is of especial interest that a chapter is devoted to the views of Michael and another to the views of Nef. In regard to the former the author says: "Without doubt, Michael's theory grasps the problems of organic chemistry in a broad way. By its aid it is possible to follow organic reactions much more in detail than formerly. Undoubtedly the further studies of Michael and his students will extend the theory especially on the quantitative side, and will in many ways simplify its use. Chemists may expect still further advances as a result of the further development of these views." It is to be hoped that the comparatively simple presentation of Michael's views will lead to a more thorough study of his original articles.

Speaking of Nef's views, the author says: "To-day Nef's proofs of the existence of compounds with bivalent carbon are pretty generally accepted. The same cannot be said of his other theoretical speculations, especially of the methylene

chemistry. Nevertheless, they are worthy of the highest consideration. They are frequently applied to reactions, especially to rearrangements, and give in such cases perhaps the most plausible explanation."

The book is cordially recommended.

I. R.

ANLEITUNG FÜR DAS ORGANISCH-PRÄPARATIVE PRAKTIKUM. Von DR. FRANZ WILHELM HENLE, früher Privatdozent an der Universität Strassburg. Mit einer Vorrede von DR. J. THIELE, Professor an der Universität Strassburg. Mit zahlreichen Skizzen. Leipzig: Akademische Verlagsgesellschaft M. b. H. 1909. Preis, brosch., M. 4.60; gebunden, M. 5.20.

This book on organic preparations has a number of excellent features not always found in such treatises. The chief one is the fine list of references to the important articles on each subject treated. One page is given to a list of the necessary first outlay of apparatus, another to precautions against various accidents, and another to the first aid to those injured by burns, cuts, or harmful chemicals or gases.

The list of preparations is about the usual one, though not so full as that in Gattermann's book. The author might have omitted some of the list of *fifteen* compounds in which a halogen is introduced, and inserted others of greater importance in their place. The various methods of separating and purifying compounds (distillation, crystallization, etc.), are described as they are needed in making the first few preparations. This method probably impresses the student more forcefully than does the consideration of these manipulations in an introduction. A large number of test tube reactions of the various substances are given, but the actual equations representing the chief reactions are unfortunately omitted. The student is much more likely to master these characteristic reactions if he can read them in the book on organic preparations while he is dealing with the substances than he is if he is forced to go to a text-book on organic chemistry.

The paper, printing, cuts of apparatus, and graphical formulas are unusually fine. Altogether this volume should meet with a very hearty reception.

S. F. ACRER.

QUANTITATIVE EXPERIMENTS IN GENERAL CHEMISTRY. By JOHN TAPPAN STODDARD, Professor of Chemistry in Smith College. New York: Longmans, Green & Co. 1908. pp. vii + 115. Price, \$1.

This is a small manual for college use containing rough quantitative experiments illustrating the gas laws, densities of gases, specific heats, air, water, analysis of some simple gaseous compounds and of many metallic oxides, sulphides and salts. The book is not written as an elementary quantitative manual for chemists, but rather as a book for students not intending further study of chemistry to impress upon

their minds the quantitative significance of chemical law. The experiments are well selected and simple. E. R.

GESÄTTIGTE SALZLÖSUNGEN VON STANDPUNKT DER PHASENLEHRE. Von DR. PHIL. ERNST JÄNECKE, Privatdozent an der Königl. Technischen Hochschule in Hannover. Mit 83 Tabellen, 153 Abbildungen im Text. Halle a. S.: Verlag von Wilhelm Knapp. 1908. pp. 187. Price, M. 9.

This book, which the author dedicates to his teacher, van't Hoff, is based upon a course of lectures delivered in 1906 at the Technical High School in Hannover.

The work of Roozeboom, Meyerhoffer and especially van't Hoff, on the conditions of equilibria in solutions of salts is very well known in general. This work is brought together in a systematic form in this monograph and treated in terms of the phase rule. This is a welcome addition to physical chemical literature. The publications of these various authors were so widely scattered through the journals as to render them difficultly accessible to many who would like to follow these investigations in some detail.

Further, the individual papers dealing with the special topics were often difficult reading for those who had not followed closely the entire literature bearing upon the problems under investigation.

A well-arranged account of the work that has been done, and is in progress in this interesting field, is now at hand.

H. C. J.

MEAT AND FOOD INSPECTION. By WM. ROBERTSON, M.D., D.P.H.F.P.S. With Regulations Governing Meat Inspection in the United States. By MAXIMILIAN HERZOG, M.D. Chicago: W. T. Keener & Company. pp. 372 + x. Price, \$3.50.

The first 146 pages of this book are devoted to the inspection of meat, chiefly from a veterinary standpoint. Two hundred and one pages are given up to the text of the laws of Great Britain and Ireland, together with brief footnotes by the author in explanation thereof and a list of the acts given and cases cited. The book makes no reference to other conditions than those of Great Britain and Ireland, except that the text of the regulations governing meat inspection in the United States is given. On the whole, the scope of the book is not such as would be indicated by its title.

W. D. BIGELOW.

ERRATA.

Vol. 42, p. 128, footnote 4, should read: Stieglitz and Acree: *Ibid.*, 39, 529.

Vol. 42, p. 129, footnote 4, should read: Stieglitz and Acree: *This JOURNAL*, 39, 529, and Stieglitz: *Ibid.*, 39, 651.